ORIGINAL CONTRIBUTION

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Nasopharyngeal endoscopic resection in the management of selected malignancies: ten-year experience*

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SUMMARY

Objective: *To evaluate the feasibility of endoscopic surgery in the management of selected nasopharyngeal cancers. Three different types of nasopharyngeal endoscopic resections (NER) are described.*

Method of study: *From January 1997 to October 2008, 17 consecutive patients (mean age: 50 years) with previously untreated (5) or recurrent nasopharyngeal tumours (12) were treated with curative intent by pure endoscopic resection. The extent of surgical resection was classified as follows: type 1 NER: resection limited to the postero-superior nasopharyngeal wall; type 2 NER: resection superiorly extended to the sphenoid sinus; type 3 NER: resection with lateral extension including the cartilaginous portion of the Eustachian tube and parapharyngeal space.*

Results: *Type 1 NER was performed in 4 cases, type 2 in 6, and type 3 in 7. No intra- or post-operative complications were observed. Mean hospitalization time was 4 days (range: 1-7). Follow-up ranged from 10 to 138 months (mean: 41,2 ± 38). At the time of writing, 12 (71%) patients were free of disease, 3 (17%) alive with disease, and 2 (12%) dead of disease.*

Conclusions: *NER is a feasible surgical technique that can be tailored in relation to tumour extension. Larger series and longer follow-up are needed to further validate the long-term results.*

Key words: endoscopic surgery, recurrence, nasopharynx, nasopharyngeal cancer, nasopharyngectomy

INTRODUCTION

Endoscopic endonasal surgery is now considered the gold standard in the management of most benign lesions of the sinonasal tract. In the last 10 years, this surgical approach has indeed emerged as a valid treatment option for selected malignant tumours [1-5]. The experience accumulated by many authors in this field, has naturally outlined the opportunity to manage also selected lesions of the nasopharynx [6-8]. It is well known that radiotherapy (RT) associated with chemotherapy (CHT) is the mainstay of treatment for nasopharyngeal carcinoma (NPC)[9]. The reasons for this are related to several aspects including the fact that most NPCs are undifferentiated or nonkeratinizing and consequently highly radiosensitive, and that the complexity of the nasopharyngeal anatomy with critical areas (internal carotid artery, skull base, parapharyngeal space) in close proximity makes radical surgery challenging and associated with dismal results [10]. Moreover, lesions are frequently diagnosed at an advanced stage. External approaches have been extensively described and codified [11-15] while only a few studies dealing with endoscopic techniques have been reported [6-8]. The improvement of the anatomical knowledge of this region, refinement of imaging techniques, and the surgical expertise acquired in sinonasal endoscopic surgery, has finally defined this approach feasible in selected cases.

In the present study, we report our experience in the management of selected recurrent and previously untreated malignant nasopharyngeal lesions by nasopharyngeal endoscopic resection (NER). The aim of the present study is to define the precise indications for such an approach, to describe different endoscopic resections in relation to tumour extent, and to report our preliminary results in terms of complications, local control and determinate survival.

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MATERIALS AND METHODS

Patients and disease staging

Between January 1997 and October 2008, 17 consecutive patients were submitted to NER: 12 patients had a recurrent disease previously treated by RT with or without concurrent CHT in 8 cases (7 NPCs, 1 adenocarcinoma), and surgery in association or not with RT and/or CHT in 4 (2 NPCs, 1 adenocarcinoma, 1 melanoma), while 5 patients were affected by previously untreated nasopharyngeal tumours (3 adenoidcystic carcinoma, 1 papillary adenocarcinoma, 1 undifferentiated sarcoma). The disease was staged according to the last UICC staging system [16]. Extension of disease was carefully evaluated by endoscopic examination and imaging studies such as computed tomography (CT) and magnetic resonance (MR). Moreover, CT or MR angiography was always obtained in order to clearly define anatomic variations of parapharyngeal and paraclival course of the internal carotid artery (ICA). When required, regional or distant dissemination of disease was preoperatively excluded by PET-CT. Patients were considered unsuitable for NER in case of intracranial spread or involvement of the orbital content, pterygoid muscles, ICA, or oropharynx.

Surgical procedure

All patients were treated with a pure endoscopic approach under hypotensive general anesthesia in a supine position. Cotton pledgets soaked in a solution composed by epinephrine 1:100.000, xylomethazoline, and carbocaine were placed into nasal cavities to reduce bleeding and improve transnasal access in terms of operative space.

The surgical procedure was initiated with the resection of the posterior third of the nasal septum (vomer) to visualize and control the entire nasopharyngeal cavity and to better handle surgical instruments through both nasal fossae. A Diomed 25 diode laser (Diomed Co., Cambridge, UK) with pulse-wave (30 watt) in contact mode was always adopted to mark the limits of the surgical resection.

Tumour resections were classified into 3 types according to the extension of disease:

Type 1 NER: the resection was limited to the postero-superior nasopharyngeal wall reaching the bony floor of the sphenoid sinus. The surgical incision began bilaterally from the nasopharyngeal vault posteriorly to the Eustachian tube, down following the posterior border of the torus into the Rosenmüller fossa, to an axial plane at the level of the atlas. The cartilaginous portion of the Eustachian tube was preserved. Posteriorly, the surgical resection deeply reached the periostium of the skull base, and the ventral portion of the clivus was always drilled out (Figure 1). In such a limited resection, the tumour was always removed en bloc with adequate and safe mucosal margins routinely checked by frozen sections.

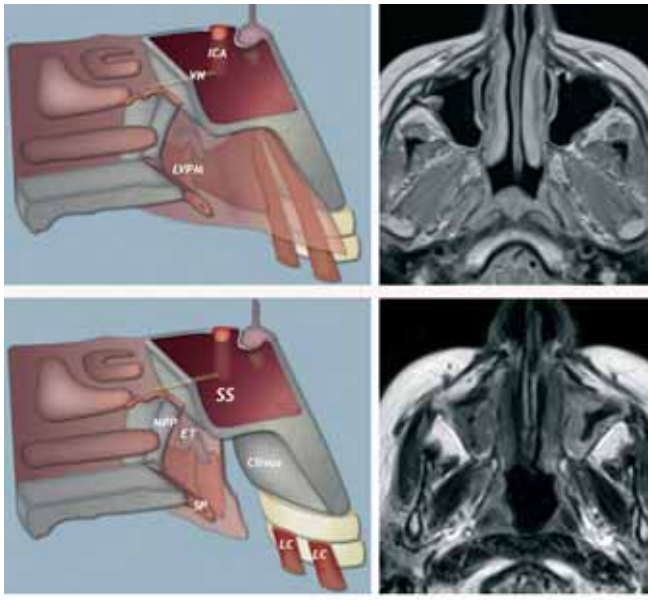

Figure 1. NER 1. On the left side, schematic drawings of a sagittal split nasopharynx underline the structures removed during the resection. On the right side, pre and postoperative MRI examination of a patient affected by adenocarcinoma limited to posterior nasopharyngeal wall.
VN-Vidian nerve; LVPM-Levator veli palatine muscle; ICA-internal carotid artery; SS-sphenoid sinus; MPP-medial pterygoid plate; ET-eustachian tube; SP-soft palate; LC-longus capitis muscle.

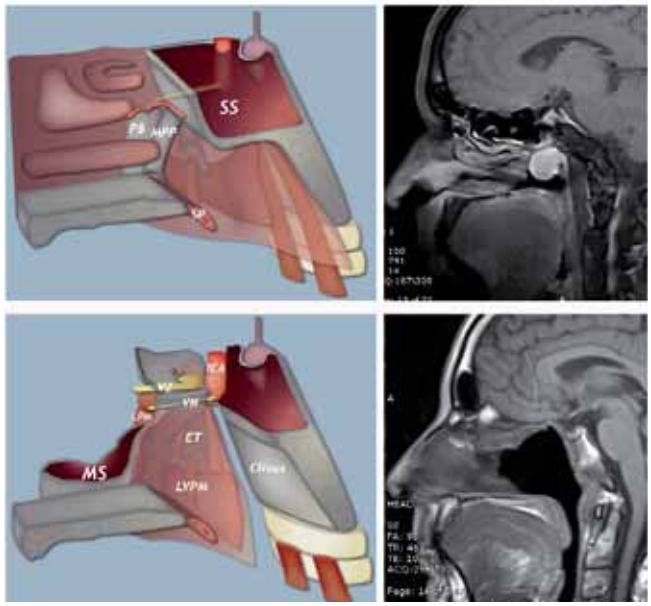

Figure 2. NER 2. On the left side, schematic drawings of a sagittal split nasopharynx underline the structures removed during the resection. On the right side, pre and postoperative MRI examination of a patient affected by recurrent nasopharyngeal carcinoma after chemo-radioterapy limited to the vault not extended to the lateral pharyngeal wall.
VN-Vidian nerve; PB-palatine bone; V2-second branch of the trigeminal nerve; LPM-lateral pterygoid muscle; LVPM-Levator veli palatine muscle; ICA-internal carotid artery; SS-sphenoid sinus; MS-maxillary sinus; MPP-medial pterygoid plate; ET-eustachian tube; SP-soft palate.

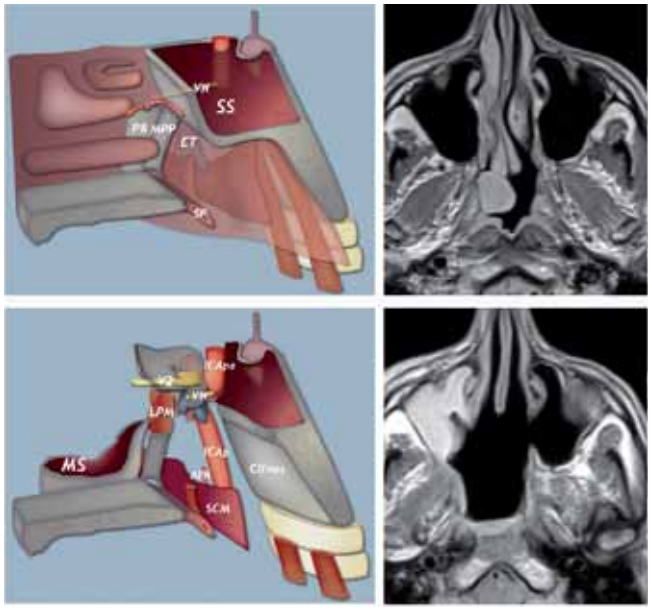

Figure 3. NER 3. On the left side, schematic drawings of a sagittal split nasopharynx underline the structures removed during the resection. On the right side, pre and postoperative MRI examination of a patient affected by adenoidcystic carcinoma involving the torus tubarius.
VN-Vidian nerve; PB-palatine bone; V2-second branch of the trigeminal nerve; LPM-lateral pterygoid muscle; ICApa-paraclival internal carotid artery; ICAp-parapharyngeal internal carotid artery; SS-sphenoid sinus; MS-maxillary sinus; MPP-medial pterygoid plate; ET-eustachian tube; SP-soft palate; APA-ascending pharyngeal artery; SCM-superior constrictor muscle.

Type 2 NER: the resection was superiorly extended to include the anterior wall and the floor of the sphenoid sinus. The posterior part of the nasal septum was removed together with the sphenoid rostrum superiorly, then the natural ostia were enlarged and both the anterior sphenoidal wall and intersphenoidal septum were removed. The sphenoidal mucosa was stripped out and the floor of the sinus was entirely drilled to the coronal plane at the level of the clivus. The cartilaginous portion of the Eustachian tube was preserved. The superior turbinate was resected to obtain a wide median sphenoidotomy. In contrast, the posterior portions of inferior and middle turbinates were removed only if required by the tumour extension. As previously explained for type I NER, the posterior surgical resection margin deeply reached the periostium of the skull base and the ventral portion of the clivus was always drilled out (Figure 2).

Type 3 NER: this approach extended laterally to include the lateral nasopharyngeal wall up to the parapharyngeal space and the ipsilateral cartilagineous portion of the Eustachian tube. On the midline, the surgical resection was similar to type 2 NER including the sphenoid floor and the posterior nasopharyngeal wall deeply reaching the periosteum of the skull base, drilling out the ventral portion of the clivus.

To obtain adequate exposure of the surgical field, the previously described resection of the nasal septum was combined with a complete ethmoidectomy and a modified medial maxillectomy with exposure of the posterior maxillary wall. The content of the pterygomaxillary fossa was subsequently exposed, and the sphenopalatine artery was identified and clipped. Finally, a transpterygoidal approach was performed by drilling at least the root of the medial pterygoid lamina having previously recognized the vidian nerve in its bony canal that guides the surgeon to the junction between the horizontal intrapetrous and vertical paraclival portion of the ICA. An angled atraumatic probe was positioned into the tube, and its cartilagineous part was removed identifying its bony portion. At this point the surgeon must take care not to damage the parapharyngeal ICA that lies just behind this anatomic landmark. When required, the floor of the middle cranial fossa and the lateral foramina (rotundum and ovale) can be reached with an extended transpterygoidal approach (Figure 3). At the end of the surgical procedure, it is strongly suggested to put in place a permanent transtympanic ventilation tube to prevent a glue ear and subsequent conductive hearing loss.
In all cases surgical margins were carefully examined with frozen sections. The wound was always left free to heal by second intention. Nasal packing was removed 24-48 hours after the operation.

RESULTS

Type 1 NER was performed in 4 cases, type 2 in 6 and type 3 in 7. In case of resection of the Eustachian tube, permanent trans-tympanic drainage was always created at the end of the surgical procedure. No intra- or postoperative complications were observed. Furthermore neither nasal reflux nor impaired swallowing were reported by any patient.
Mean hospitalization time was 4 days (range: 1-7), and all patients were discharged with nasal irrigation with saline solution and topic antibiotic therapy. The lesions were staged according to UICC TNM staging system classification [16] as follows: stage I, 10 (59%), stage II, 2 (12%), stage III, 3 (17%)

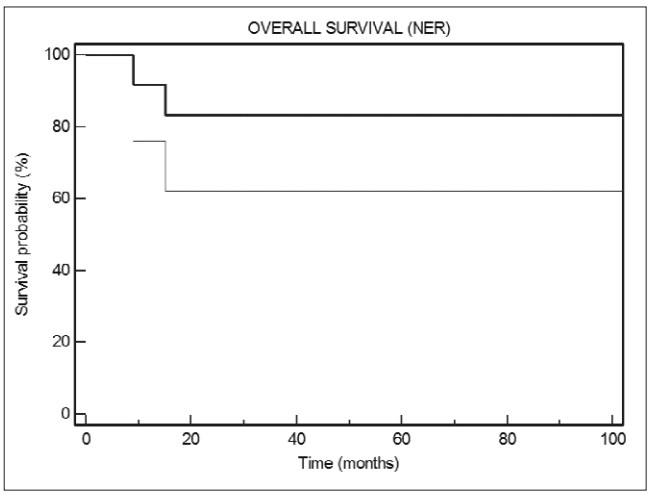

Figure 4. Kaplan Meier survival curve: Overall survival.

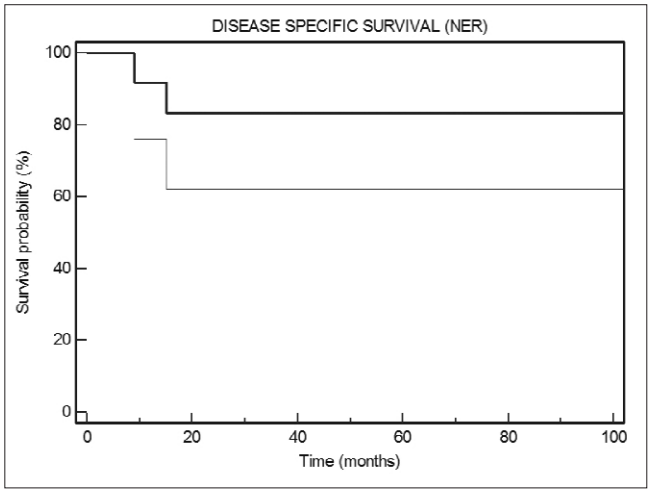

Figure 5. Kaplan Meier survival curve: Disease specific survival.

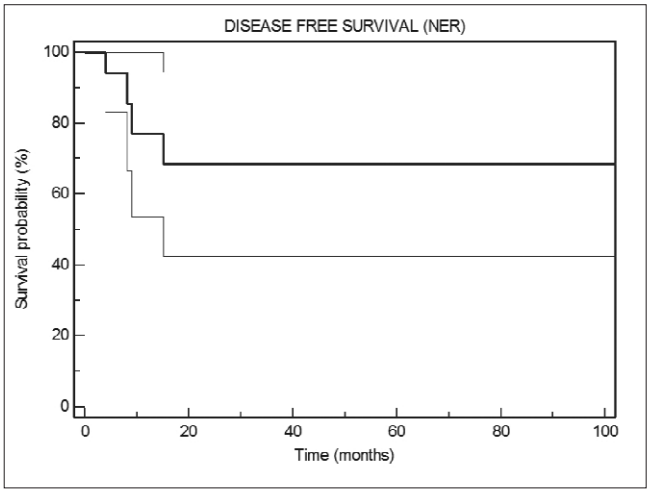

Figure 6. Kaplan Meier survival curve: Disease free survival.

and stage IV, 2 (12%). Postoperative adjuvant treatment was delivered in 5 cases including RT in the 3 previously untreated cases of adenoid cystic carcinomas and CHT in 2 extended recurrent nasopharyngeal tumours. The follow-up period ranged from 10 to 138 months (mean: 41,2 ± 38 SD). At the time of last follow-up, 12 (71%) patients were free of disease, 3 (17%) alive with disease and 2 (12%) dead of disease (one from sarcoma, probably induced by previous radiation, and the other from a second recurrence of a NPC). Survival curves related to overall survival, disease specific survival and disease free survival are shown in Figures 4, 5 and 6. Kaplan-Meier analysis seems to demonstrate, although our sample size is limited, that most failures (death or recurrence) happen in the first two years. Furthermore, given the fact that in our series all the deaths are related to the disease, overall survival coincides with disease specific survival. Unfortunately no significant evaluation can be proposed regarding the role of histopathology even if this aspect could be one of the most important affecting outcomes. Detailed data of the patients are summarized in Table 1.

DISCUSSION

NPC is the most frequent tumour arising in the nasopharynx. Most NPCs are poorly differentiated or undifferentiated neoplasms and consequently suitable for RT delivered with curative intent. In particular, for these histotypes, RT eventually

Table 1. Data of the patients.

N° patient	Age	Sex	Histology	Grading	Ner	F.u.	Days in Hospital	Previous treatment	Pt	Pn	Post-op treatment	Results
1	30	f	adenoidcystic carcinoma	G1	2	138	7	0	T2a	N0	RT	AWD
2	70	f	adenocarcinoma	G1	2	103	3	RT	rT1	N0	0	NED
3	55	m	adenoidcystic carcinoma	G1	3	85	4	0	T4	N0	RT	NED
4	48	m	NPC	-	3	78	5	CHT + RT + CH	rT3	N1	CHT	AWD
5	70	f	adenocarcinoma	G2	2	56	6	CH + RT	rT1	N0	0	NED
6	34	f	NPC	-	3	40	2	CHT + RT	rT1	N0	0	NED
7	70	m	NPC	-	2	32	5	CHT + RT	rT3	N0	CHT	AWD
8	51	m	NPC	-	3	28	3	CHT + RT	rT2a	N0	0	NED
9	75	m	plasmocitoma	-	1	28	1	RT	rT1	N0	0	NED
10	37	m	papillary adenocarcinoma	G1	1	21	1	0	T1	N0	0	NED
11	64	m	undifferentiated sarcoma	-	1	21	3	0	T1	N0	0	DOD
12	57	m	NPC	-	2	15	7	CH + RT	rT3	N0	0	DOD
13	59	m	NPC	-	3	12	5	CHT + RT	rT1	N0	0	NED
14	60	m	melanoma	-	1	12	6	CH	rT1	N0	0	NED
15	39	m	NPC	-	3	12	3	CHT + RT	rT1	N0	0	NED
16	62	f	NPC	-	2	10	4	RT	rT1	N0	0	NED
17	43	m	adenoidcystic carcinoma	G1	3	10	4	0	T4	N0	RT	NED

NPC: nasopharyngeal carcinoma; NER: nasopharyngeal endoscopic resection; CHT: chemoterapy; CH: surgery; RT: radiotherapy; NED: no evidence of disease; DOD: died of disease; AWD: alive with disease

associated with CHT is now considered the mainstay of treatment. In recent years, salvage surgery is considered a feasible option in case of failures, and more recently endoscopic procedures have emerged as a possible alternative to traditional external approaches as salvage treatment for selected recurrent, unresponsive tumours. As a valuable option, NER might also be considered as a primary treatment modality for selected lesions that are not suitable for RT.

From an anatomical point of view, the nasopharynx represents one of the most challenging and complex areas to reach, surgically manage and dissect. Different external approaches for nasopharyngectomy have been described including infratemporal fossa [11], anterolateral disassembly [15], maxillary and mandibular swings [14] or transpalatal approaches [13]. However, all these approaches are troublesome, and are always associated with prolonged hospitalization and morbidity that should not be underestimated.
A more physiological way to reach the nasopharynx is by passing through the nasal fossae, even if this possibility has not been clinically and surgically explored until recent years, because of limitations in surgical instrumentation and lack of sufficient anatomical knowledge. In this prospective, endoscopic procedures have opened new and innovative surgical possibilities. Improvements in surgical skills, anatomical knowledge, dedicated instrumentations and neuronavigation systems have permitted endoscopic surgeons to treat various pathologies, even those located far laterally in the nasopharynx such as inflammatory diseases of the petrous apex [17].

In this study, we report our preliminary experience with NERs. Endoscopic procedures have been traditionally considered unsatisfactory in reaching adequate and safe surgical margins, especially for malignancies. This preconception is slowly changing with the progressive definition of clear indications and codified approaches like multilayer centripetal resection [1-5]. In spite of encouraging oncological results, many experienced surgeons still believe that larger approaches are equated with better outcomes. In contrast, an endoscopic approach is limited only by access to the surgical field, with the opportunity to precisely control, in properly selected cases, resection margins and relationships with critical areas thanks to magnification, angled telescopes and the use of dedicated instruments such as intraoperative doppler and neuronavigation systems. Furthermore, with this approach there is no need for external incisions or unnecessary osteotomies. The surgical resection can be modulated in relation to the tumour extent, and thus tailored to the specific needs of the patient. The anatomic limits for safe nasopharyngeal resection are the dura of the posterior cranial fossa posteriorly and ICAs laterally. We stress the crucial role of preoperative imaging evaluation, which needs to be discussed with an experienced radiologist to properly plan the surgical resection and evaluate the relation between the tumour and critical structures. In almost all cases of the present series, CT angiography was performed to evaluate possible variations of natural course of the parapharyngeal ICA, always associated with traditional CT and MR images. The major risk in this kind of approach is possible ICA damage during infratemporal parapharyngeal dissection. From an anatomical point of view, we underline the role of the bony part of the Eustachian tube as a useful landmark in detecting the parapharyngeal portion of the ICA, and emphasize how probing of the tube allows the operator to not overrun the coronal plane behind which the ICA is located.

Preliminary evaluation of our results concerning endoscopic management of NPC recurrences, perioperative complications and local control is in agreement with previously reported experiences [6-8] and permits additional considerations. We trust that it is too early to perform a meaningful statistical evaluation, taking into account the small size of the patient cohort, the heterogeneous group of histotypes and the relative shortness of follow-up. Notwithstanding, although with these well-known limitations, a survival analysis seems to demonstrate that most failures (death or recurrence) happen in the first two years. Furthermore, in our series overall survival coincides with disease specific survival given the fact all the deaths observed are related to the disease. The prognostic role of the histological type cannot be extrapolated from our data; in this sense greater number of patients make us understand in the future if the biological behaviour of the tumour is one of the most important factor affecting the outcome, as it happens in other districts. Nevertheless, our data substantiate the feasibility and good tolerability of such approaches. In this regard, the Hippocratic concept of “primum non nocere” is the leading rule that drives our clinical experience. In fact, the aim of our retrospective evaluation was not to provide new guidelines for management of such complex scenarios, but to adequately delineate the practical aspects of these surgical procedures and to demonstrate their utility in selected cases. This latter aspect is particularly true in cases for which no suitable therapeutic options can be considered and in which the natural course of the disease affects the quality of life even more than an extensive surgical procedure would do.

CONCLUSION

These preliminary results show that NER is a feasible surgical technique in the treatment of selected nasopharyngeal tumours, which can be modulated in relation to tumour extension. This approach may be considered a suitable option, even if a larger series of patients and longer follow-up are needed to better define the role of NER in the treatment of these lesions.

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