

# Anatomical studies and early results on endoscopic transoral medial pterygomandibular fold approach to salvage retropharyngeal lymphadenectomy in nasopharyngeal carcinoma

## Main Article

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### Abstract

**Objective.** Retropharyngeal lymphadenectomy is challenging. This study investigated a minimally invasive approach to salvage retropharyngeal lymphadenectomy in patients with nasopharyngeal carcinoma.

**Methods.** An anatomical study of four fresh cadaveric heads was conducted to demonstrate the relevant details of retropharyngeal lymphadenectomy using the endoscopic transoral medial pterygomandibular fold approach. Six patients with nasopharyngeal cancer with retropharyngeal lymph node recurrence, who underwent retropharyngeal lymphadenectomy with the endoscopic transoral medial pterygomandibular fold technique at the Eye and ENT Hospital of Fudan University from July to December 2021, were included in this study.

**Results.** The anatomical study demonstrated that the endoscopic transoral medial pterygomandibular fold approach offers a short path and minimally invasive approach to the retropharyngeal space. The surgical procedure was well tolerated by all patients, with no significant post-operative complications.

**Conclusion.** The endoscopic transoral medial pterygomandibular fold approach is safe and efficient for retropharyngeal lymphadenectomy.

## Introduction

Nasopharyngeal carcinoma (NPC) is the most common head and neck cancer in southern China, occurring more frequently in Southeast Asia than elsewhere. The annual incidence of NPC in Southern China is about 30 cases per 100 000 people.<sup>1</sup> The retropharyngeal lymph nodes, an extensive lymphatic network, are widely considered the first-echelon lymph nodes for the nasopharynx.<sup>2</sup> Therefore, metastatic retropharyngeal lymph nodes are a common phenomenon in NPC patients, with an incidence rate of 64.2–75.1 per cent.<sup>3–5</sup> In the eighth American Joint Committee on Cancer/Union for International Cancer Control staging system, retropharyngeal lymph node metastasis was classified as nodal N<sub>1</sub> stage.<sup>5</sup> The occurrence of retropharyngeal lymph node metastasis was considered an unfavourable prognostic factor in NPC patients.<sup>6</sup>

Radiotherapy is the mainstay treatment for primary NPCs, as it is sensitive to radiation. The target areas usually also include metastatic retropharyngeal lymph nodes.<sup>7</sup> However, re-irradiation is not ideal for retropharyngeal lymph node recurrence because of radioresistance and severe radiotoxicity. In addition, the adjacent normal tissues have already absorbed radiation doses near tolerance from previous radiotherapy. Therefore, salvage treatment of recurrent or residual retropharyngeal lymph nodes is more challenging and complicated than primary retropharyngeal lymph node metastasis.

The National Comprehensive Cancer Network guidelines for recurrent NPC recommend surgery as a first-line salvage treatment for patients with resectable tumours.<sup>8</sup> Compared to re-irradiation, surgery can improve local control and increase survival rates without causing major long-term complications. Resection of masses in the retropharyngeal space is complex because of its anatomical complexity and proximity to the internal carotid artery. Retropharyngeal lymphadenectomy for recurrent or residual retropharyngeal lymph nodes in NPC is more difficult than in other tumours because of the

local reaction after radiation. As a result, such operations are performed only in a few hospitals.

Retropharyngeal lymphadenectomy of retropharyngeal lymph nodes in NPC patients has been reported in only a few articles.<sup>9–11</sup> The transcervical and maxillary swing approaches are traditionally used for retropharyngeal lymphadenectomy in NPC patients. However, the transcervical approach requires a long path to access the lesion. Moreover, injury to the lower cranial nerves and pharyngocutaneous fistulas may sometimes occur. The maxillary swing approach can cause serious surgical complications such as facial scarring, trismus, palatal defect, dysphagia, osteomyelitis and osteonecrosis. Recently, the transcervical endoscopic approach and transoral robotic retropharyngeal lymph node dissection have been developed.<sup>10,11</sup> Although the transcervical endoscopic approach is assisted by endoscopy, nerve injury and pharyngeal fistulas are still common.<sup>11</sup> For transoral robotic retropharyngeal lymph node dissection, it is sometimes difficult to precisely locate the retropharyngeal lymph node. Furthermore, high medical costs, a lack of tactile sense, the amount of time needed, a lack of robotic equipment, and the extensive hand–eye co-ordination training required prevent the widespread adoption of surgical robotics.<sup>12</sup>

This study introduces a novel endoscopic transoral medial pterygomandibular fold approach, for a minimally invasive procedure with fewer complications, for retropharyngeal lymphadenectomy in NPC patients. We first demonstrate the relevant details in a step-by-step anatomical study. Furthermore, we present our early experience in managing six cases, to aid understanding of the technical nuances.

## Materials and methods

The study was approved by the institutional review board of the Eye and ENT Hospital of Fudan University. Eight sides of four fresh cadaveric heads were dissected for the anatomical study, after injecting coloured liquid silicone into the arterial and venous beds (red and blue, respectively). Endoscopic endonasal surgery instruments (Storz Endoscopy, Tuttlingen, Germany) and the Coblator Surgery System (ArthroCare, Sunnyvale, California, USA) were used for dissection and surgical procedures. The procedures were performed using a 0° endoscope (Karl Storz; 4 mm diameter, 18 cm length) connected to a high-definition camera for visualisation and recording.

### Anatomical dissections

At the beginning of the dissection, a Davis mouth gag was used to open the mouth and expose the lateral wall of the oropharynx. A vertical mucosal and submucosal incision was made medial to the pterygomandibular fold on the soft palate with a knife blade. The fascia and the superior pharyngeal constrictor muscle were dissected. The muscles, fat tissues, vessels and nerves in the parapharyngeal space were then exposed and identified. Finally, the retropharyngeal space was exposed. Anatomical structures were photographed and recorded.

### Case series

This study included six nasopharyngeal carcinoma patients with retropharyngeal lymph node recurrence, who were treated at the Eye and ENT Hospital of Fudan University from July 2021 to December 2021. Demographic and clinical

characteristics were collected, including gender, age, history, treatments, radiographic findings, retropharyngeal lymph node size, internal carotid artery involvement, balloon occlusion test findings, surgical approaches, complications, pathological findings and follow-up results.

The extent of the tumour and its relationship with the adjacent vital structures were evaluated by pre-operative computed tomography and enhanced magnetic resonance imaging (MRI) plus magnetic resonance angiography. Enhanced MRI images were obtained on the 1st post-operative day to evaluate the extent of resection following surgery.

All patients were fully informed about the surgical procedures and associated risks. Furthermore, they were informed and counselled about the possible need to convert to external approaches.

## Results

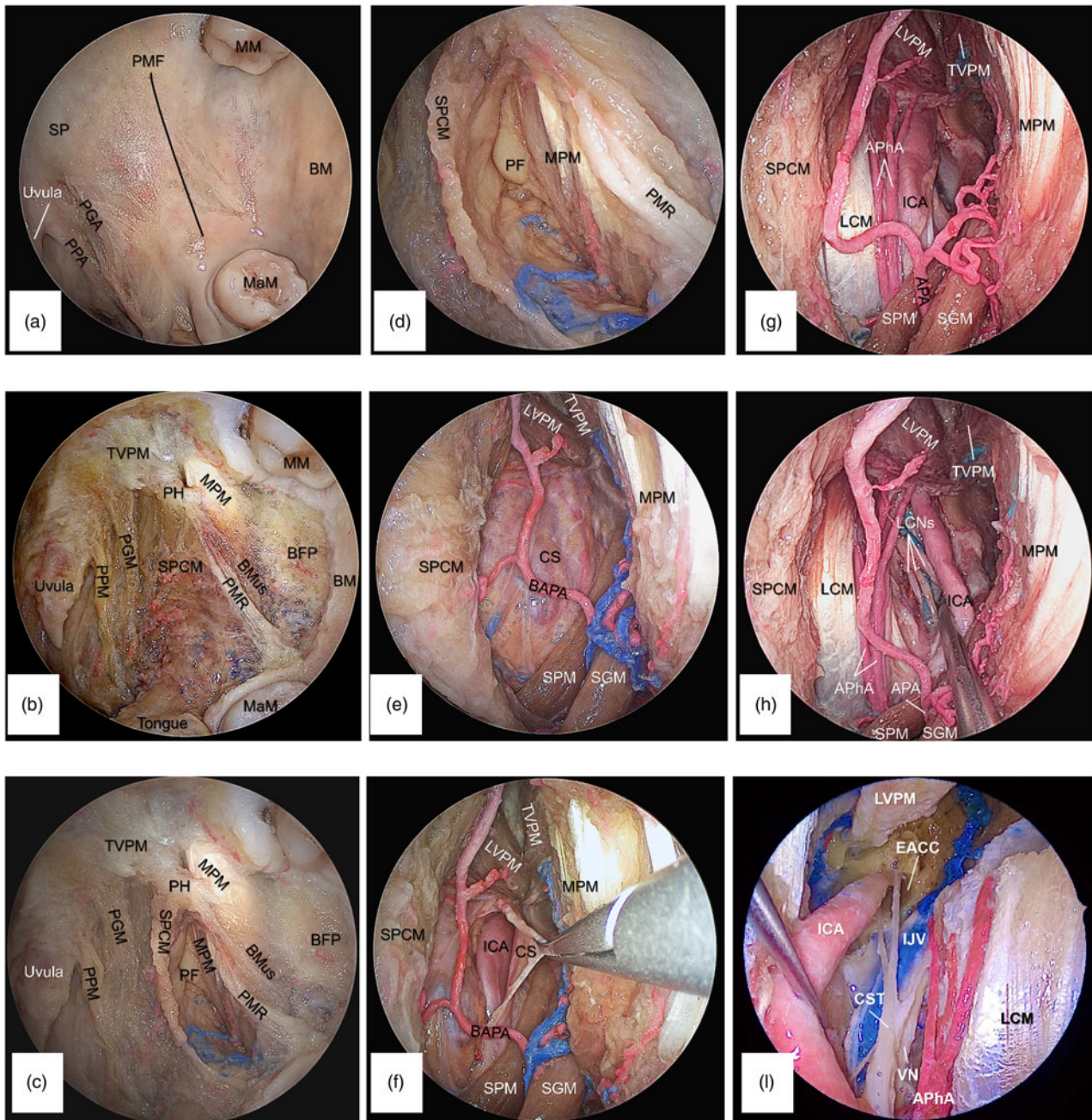
### Anatomy

The tissue layers of the mucosa and submucosa were meticulously separated to reveal the superior pharyngeal constrictor muscle and the pterygomandibular raphe in every specimen. Subsequently, the superior pharyngeal constrictor muscle was dissected, exposing the prestyloid fat, and the ascending palatine artery, along with its branches located in the prestyloid space. The tensor veli palatini muscle and the pterygoid hamulus were revealed superiorly, whereas the medial pterygoid muscle was shown laterally. The fat and vascular vessels were removed to reveal the styloglossal muscle and the stylopharyngeal muscle in the prestyloid space's lower portion. The carotid sheath was evident immediately behind the stylopharyngeal muscle. The process continued posteriorly along the superior pharyngeal constrictor muscle's lateral surface, exposing the longus capitis muscle. Following the dissection of the carotid sheath, both the internal carotid artery (ICA) and ascending pharyngeal artery were exposed. The retropharyngeal lymph node was then identified, lying between the longus capitis muscle and the ICA. The subsequent resection of the retropharyngeal lymph node and the lateral displacement of the ICA revealed the cervical sympathetic trunk situated posteriorly to the ICA (Figure 1).

### Case series

The basic demographic and clinical characteristics of the included cases are shown in Table 1. Each patient had a history of nasopharyngeal carcinoma (NPC), and had undergone radiotherapy with chemotherapy. The interval between retropharyngeal lymph node recurrence and the original diagnosis of NPC ranged from 12 to 32 months, with a mean interval of 18 months. Patient number four also underwent two other surgical procedures because of tumour recurrence in the nasopharynx; the first procedure was an endoscopic endonasal extended nasopharyngectomy repaired with a temporalis muscle flap, and the second procedure was an endoscopic endonasal extended nasopharyngectomy.

Enhanced MRI plus magnetic resonance angiography scans demonstrated that the minimal axial diameter of retropharyngeal lymph node was 6 mm or larger except in case six (5.6 mm). All enlarged retropharyngeal lymph nodes were closely related to the ICAs. The ipsilateral ICA in case two was encased by the retropharyngeal lymph node. The recurrent tumours were staged as shown in Table 1, according to



**Figure 1.** Anatomical dissections of the endoscopic transoral medial pterygomandibular fold approach to the retropharyngeal space of two cadaveric heads, one from the left side (a–h), and one from the right side (i). (a) The pterygomandibular fold (solid line) was identified on the left side of the soft palate. The pterygomandibular fold indicated the submucosal location of pterygomandibular raphe. (b) Mucosa of the soft palate was removed. The superior pharyngeal constrictor muscle and the buccal muscle were identified, and between them was the pterygomandibular raphe. The superior attachment point of the pterygomandibular raphe was pterygoid hamulus. The tensor veli palatini muscle rounded the pterygoid hamulus and extended medially to palatine aponeurosis. The medial pterygoid muscle was lateral to the pterygoid hamulus and ran inferolaterally. The palatoglossal muscle and palatopharyngeal muscle were located medially to the superior pharyngeal constrictor muscle and fused. (c) The superior pharyngeal constrictor muscle was dissected along the vertical line medial to the pterygomandibular raphe. The prestyloid fat and the medial surface of the lower part of the medial pterygoid muscle were exposed in the parapharyngeal space. (d) Enlarged view of (c). (e) The prestyloid fat in the parapharyngeal space was carefully removed. The levator veli palatini muscle and tensor veli palatini muscle were shown superiorly, the styloglossal muscle and stylopharyngeus muscle inferiorly, the medial pterygoid muscle laterally, and the superior pharyngeal constrictor muscle medially in this dissection field. The tensor veli palatini muscle was located between the medial pterygoid muscle and the levator veli palatini muscle. The branch of ascending palatine artery originated from the ascending palatine artery, and gave branches to the superior pharyngeal constrictor muscle and levator veli palatini muscle. The carotid sheath was revealed between the levator veli palatini muscle and stylopharyngeus muscle. (f) After dissection of the carotid sheath, the internal carotid artery (ICA) was identified. (g) The branch of ascending palatine artery and its branches were pulled medially, and the carotid sheath, prevertebral fascia and veins were removed carefully to expose the ascending palatine artery, ascending pharyngeal artery and longus capitis muscle. The ascending palatine artery ascended between the styloglossal muscle and the stylopharyngeus muscle. The ascending pharyngeal artery was between the longus capitis muscle and the ICA. (h) The ICA was retracted laterally to expose the lower cranial nerves. (i) Right side of another cadaveric head. The ICA was pulled laterally to show the cervical sympathetic trunk, which was posterior to the ICA. APA = ascending palatine artery; APhA = ascending pharyngeal artery; BAPA = branch of ascending palatine artery; BFP = buccal fat pad; BM = buccal mucosa; BMus = buccal muscle; CS = carotid sheath; CST = cervical sympathetic trunk; ICA = internal carotid artery; IJV = internal jugular vein; EACC = external aperture of the carotid canal; LCM = longus capitis muscle; LCNs = lower cranial nerves; LVPM = levator veli palatini muscle; MaM = mandibular molar; MM = maxillary molar; MPM = medial pterygoid muscle; PF = prestyloid fat; PGA = palatoglossal arch; PGM = palatoglossal muscle; PH = pterygoid hamulus; PMF = pterygomandibular fold; PMR = pterygomandibular raphe; PPA = palatopharyngeal arch; PPM = palatopharyngeal muscle; SGM = styloglossal muscle; SP = soft palate; SPCM = superior pharyngeal constrictor muscle; SPM = stylopharyngeus muscle; TVPM = tensor veli palatini muscle; VN = vagus nerve

**Table 1.** Demographic and clinical characteristics

Case no.	Sex/age (years)	Interval* (months)	RPLN size (mm)	ICA involvement	Clinical rTNM stage	Operation (side)	En bloc or intracapsular resection	NG tube?	Pathology	Post-op complications	Patient status	Follow-up duration (months)
1	F/64	12	10.2 × 20.3	Adjacent	rT <sub>3</sub> N <sub>1</sub> M <sub>0</sub>	Extended nasopharyngectomy (R) + pedicled nasoseptal flap + retropharyngeal lymphadenectomy (L)	En bloc	No	Metastatic LN	Excess effusion in operative cavity	Alive, NED	12
2	M/53	16	13.2 × 26.4	Encased	rT <sub>0</sub> N <sub>1</sub> M <sub>0</sub>	Retropharyngeal lymphadenectomy (L)	En bloc	No	Metastatic LN	Horner syndrome	Alive, NED	10
3	M/46	13	6.3 × 9.9	Adjacent	rT <sub>0</sub> N <sub>1</sub> M <sub>0</sub>	Retropharyngeal lymphadenectomy (L)	En bloc	No	Metastatic LN	None	Alive, NED	9
4	M/49	32	20.5 × 23.4	Adjacent	rT <sub>0</sub> N <sub>1</sub> M <sub>0</sub>	Retropharyngeal lymphadenectomy (L)	En bloc	No	Metastatic LN	None	Alive, NED	8
5	M/40	21	7.7 × 14.3	Adjacent	rT <sub>0</sub> N <sub>1</sub> M <sub>0</sub>	Retropharyngeal lymphadenectomy (L)	Intracapsular resection	Yes	Metastatic LN	None	Alive, NED	7
6	F/65	13	5.6 × 13.5	Adjacent	rT <sub>1</sub> N <sub>1</sub> M <sub>0</sub>	Extended nasopharyngectomy (B) + pedicled nasoseptal flap + retropharyngeal lymphadenectomy (R)	En bloc	Yes	Reactive LN	None	Alive, NED	7

\*Interval between retropharyngeal lymph node recurrence and the original diagnosis of nasopharyngeal carcinoma. No. = number; RPLN = retropharyngeal lymph node; ICA = internal carotid artery; rTNM = recurrent tumour–node–metastasis; NG = nasogastric; post-op = post-operative; F = female; R = right; L = left; LN = lymph node; NED = no evidence of disease; M = male; B = bilateral

the eighth edition of the American Joint Committee on Cancer staging for NPC.

The ipsilateral balloon occlusion test was performed under local anaesthesia in the hybrid operating theatre. The balloon occlusion test results were negative in all six patients. The balloon guiding catheter was reserved in the common carotid artery in case of an ICA blowout. The surgical procedures were then performed with the patient lying supine with oral tracheal intubation under general anaesthesia.

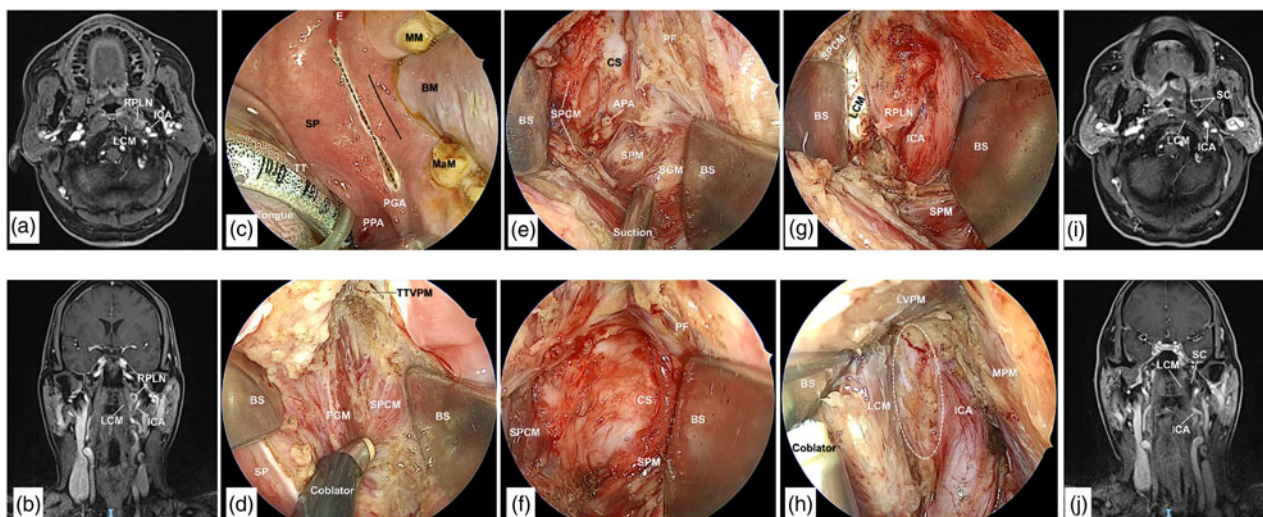
All the patients underwent retropharyngeal lymphadenectomy through the endoscopic transoral medial pterygomandibular fold approach. Two patients with a recurrent tumour in the nasopharynx were treated with extended nasopharyngectomy, and the surgical field was reconstructed with a pedicled nasoseptal flap before retropharyngeal lymphadenectomy was performed. All retropharyngeal lymph nodes were successfully located during surgery and removed. In five cases, en bloc retropharyngeal lymph node resection was performed. However, because of severe adhesion to the ICA, an intracapsular resection was executed only in case five. Post-operative imaging confirmed the complete resection of retropharyngeal lymph nodes in each case. Pathological analysis revealed retropharyngeal lymph node metastasis in five cases, with the sixth case presenting reactive lymph node hyperplasia. There was no need for transition to an external surgical approach in any of the cases. For two patients, a nasogastric feeding tube was retained for a fortnight. All patients were extubated post-operatively, with none requiring a tracheostomy.

Patients responded favourably to the surgical procedures, and tolerability was satisfactory. A slight effusion within the surgical cavity was observed in most patients in the initial post-operative days, but this resolved without additional intervention, excluding the first case. This patient (case one) required drainage of the effusion after four weeks; however, the bacterial cultures of the effusion did not show colony growth. Horner syndrome was identified in the second case, but conservative treatment strategies led to recovery within a month. Overall, patients' recovery was notable, with no significant post-operative complications reported. Furthermore, no recurrence instances were recorded during a follow-up period ranging from 7 to 12 months.

**Illustrative cases**

This section describes retropharyngeal lymphadenectomy using an endoscopic transoral medial pterygomandibular fold procedure.

Figure 2 shows the example of case two, in which pre-operative enhanced MRI showed an enlarged left retropharyngeal lymph node located between the longus capitis muscle and the ICA (Figures 2a and b). In the first stage of the operation, a Davis mouth gag was used to open the mouth and expose the lateral wall of the oropharynx. Then, a vertical incision was made medially to the pterygomandibular fold with an electric needle. The superior pharyngeal constrictor muscle was exposed and dissected to expose the parapharyngeal space. The prestyloid fat was removed, and the medial pterygoid muscle, superior pharyngeal constrictor muscle, styloid muscle group (stylopharyngeal muscle and styloglossal muscle) and levator veli palatini muscle were exposed laterally, medially, inferiorly and superiorly, respectively. The ascending palatine artery was revealed between the styloglossal muscle and the stylopharyngeal muscle. It was blocked with bipolar cautery. The dissection was continued posteriorly along the



**Figure 2.** Pre-operative imaging examination, surgical procedures and post-operative imaging examinations of case two. (a & b) Pre-operative enhanced magnetic resonance imaging (MRI) showed an enlarged left retropharyngeal lymph node located between the longus capitis muscle and the internal carotid artery (ICA). (a) Axial plane. (b) Coronal plane. (c–h) Left retropharyngeal lymphadenectomy by endoscopic transoral medial pterygomandibular fold approach. (c) A vertical incision (dotted line) was performed medial to the pterygomandibular fold (solid line) after opening the patient's mouth with a Davis mouth opener. (d) The superior pharyngeal constrictor muscle and palatoglossal muscle and tendon of the tensor veli palatini muscle were exposed after removing the submucosal tissues. The tendon of the tensor veli palatini muscle was revealed in the upper part of the surgical field. (e) The superior pharyngeal constrictor muscle was dissected and pulled medially. The styloglossal muscle, stylopharyngeus muscle and ascending palatine artery were exposed following removal of prestyloid fat. The carotid sheath was posterior to the stylopharyngeus muscle. (f) The stylopharyngeus muscle was laterally retracted to expose the carotid sheath. (g) The carotid sheath was opened to expose the ICA and the lateral margin of the retropharyngeal lymph node. The dissection was continued along the lateral surface of the superior pharyngeal constrictor muscle to expose the longus capitis muscle, which was the medial margin of the retropharyngeal lymph node. (h) The retropharyngeal lymph node was dissected in an en bloc style. The dotted oval shows the surgical field after resection of the retropharyngeal lymph node. (i) The incision was sutured in a mattress suture style. (i & j) Post-operative enhanced MRI showed the retropharyngeal lymph node was resected completely. (i) Axial MRI plane showed the surgical cavity, longus capitis muscle and ICA. (j) Coronal MRI plane showed the surgical cavity between longus capitis muscle and ICA. APA = ascending palatine artery; BM = buccal mucosa; BS = brain spatula; CS = carotid sheath; E = electrotome; ICA = internal carotid artery; LCM = longus capitis muscle; LVPM = levator veli palatini muscle; MaM = mandibular molar; MM = maxillary molar; MPM = medial pterygoid muscle; PF = prestyloid fat; PGA = palatoglossal arch; PGM = palatoglossal muscle; PPA = palatopharyngeal arch; RPLN = retropharyngeal lymph node; SC = surgical cavity; SGM = styloglossal muscle; SP = soft palate; SPCM = superior pharyngeal constrictor muscle; SPM = stylopharyngeal muscle; TT = tracheal tube; TTVPM = tendon of tensor veli palatini muscle

lateral surface of the superior pharyngeal constrictor muscle to expose the longus capitis muscle, which indicated the medial margin of the retropharyngeal lymph node. The carotid sheath was dissected to expose the ICA and the lateral margin of the retropharyngeal lymph node. The ascending pharyngeal artery was then coagulated. The retropharyngeal lymph node was separated and resected from the surrounding tissues. The incision of the soft palate was sutured in three layers, including the mucosa, submucosal tissue and the superior pharyngeal constrictor muscle; they were sutured in a mattress fashion. Complete tumour excision was confirmed by post-operative enhanced MRI on the 1st post-operative day.

The procedures of other patients were similar to that described above. Figures 3 and 4 show the pre-operative imaging, surgical procedures and post-operative imaging examinations of another two illustrative cases (cases one and six, respectively), demonstrating all the anatomical landmarks of this approach. The pre- and post-operative enhanced MRI scans confirmed total resection of the retropharyngeal lymph nodes.

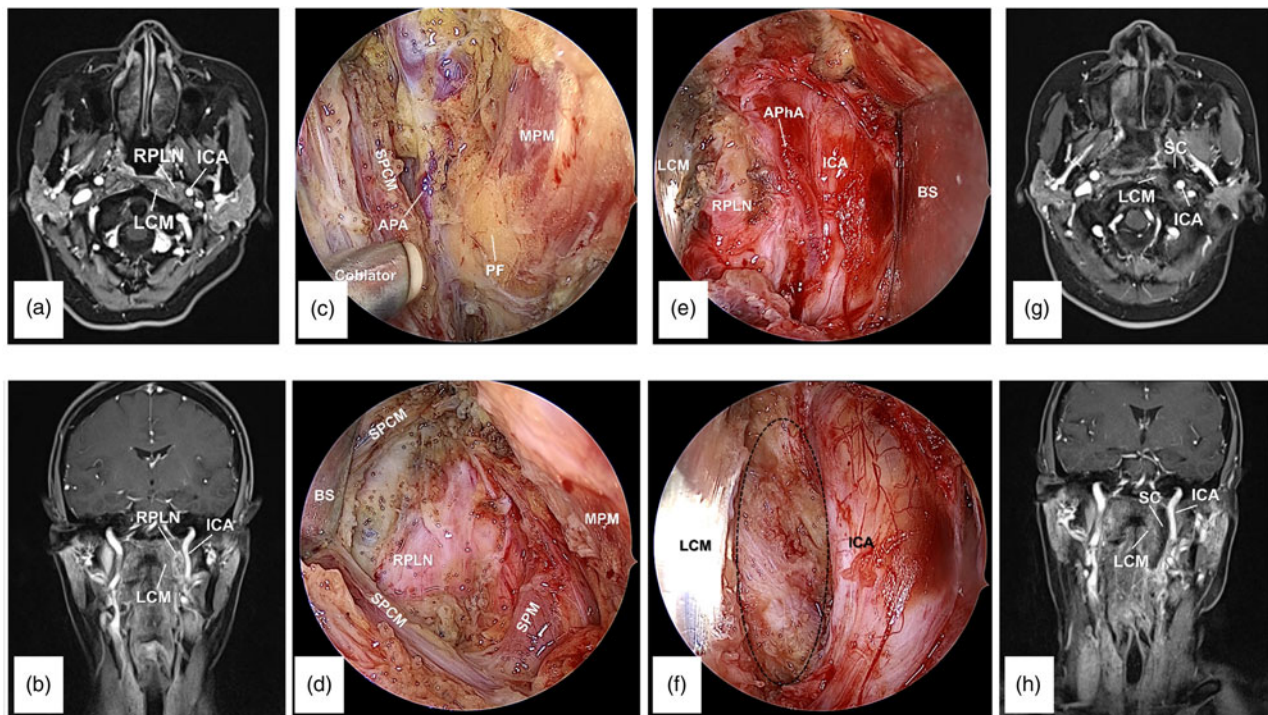
## Discussion

Retropharyngeal space is anteriorly bound by buccopharyngeal fascia, posteriorly by alar fascia, laterally by carotid sheath,<sup>13,14</sup> superiorly by the skull base and inferiorly by the space that continues to the level of vertebra C3 at its caudal extent.<sup>13</sup> It communicates with the parapharyngeal space anterolaterally.<sup>10</sup> The retropharyngeal lymph nodes lie in the retropharyngeal space medial to the internal carotid artery (ICA) and the sympathetic trunk.<sup>14,15</sup> They are traditionally

divided into two groups: medial and lateral. The lateral retropharyngeal lymph nodes, which are also called Rouvière lymph nodes, are frequently located at the level of the transverse process of the atlas,<sup>16</sup> and almost all lateral retropharyngeal lymph nodes in patients with nasopharyngeal squamous cell carcinoma are located above the level of the axis (the second cervical vertebra).<sup>17</sup> The medial retropharyngeal lymph nodes are located medial to the lateral retropharyngeal lymph nodes and consist of two groups: upper and lower.<sup>15</sup> Metastatic lateral retropharyngeal lymph nodes can normally be found. On conventional imaging, the medial retropharyngeal lymph nodes are usually small and not visible.<sup>18</sup> The presence of medial retropharyngeal lymph nodes is generally considered pathological.<sup>13,19</sup>

In retropharyngeal lymph nodes, afferent vessels originate from the ethmoid and sphenoid sinuses, posterior nasal cavity, nasopharynx, posterior pharyngeal wall, and hard and soft palate. These areas are located near the retropharyngeal lymph nodes. The afferent vessels of retropharyngeal lymph nodes also originate from the posterior capsule of the thyroid gland, the post-cricoid area and the cervical oesophagus, some distance from the retropharyngeal lymph nodes.<sup>15</sup> Therefore, retropharyngeal lymph node metastasis can result from almost any head and neck malignancy.<sup>15,20–22</sup> The most common primary tumour that leads to retropharyngeal lymph node metastasis is nasopharyngeal carcinoma (NPC).<sup>13</sup> The incidence of retropharyngeal lymph node metastasis in primary squamous cell carcinoma of the head and neck is between 4.4 and 44.1 per cent.<sup>22</sup>

Retropharyngeal lymph nodes are not routinely dissected in the classical radical, modified or selective neck dissections,<sup>13</sup>



**Figure 3.** Pre-operative imaging examination, surgical procedures and post-operative imaging examinations of case one. (a & b) Pre-operative enhanced magnetic resonance imaging (MRI) showed an enlarged left retropharyngeal lymph node located between the longus capitis muscle and the internal carotid artery (ICA). (a) Axial plane. (b) Coronal plane. (c–f) Left retropharyngeal lymph node dissection using the endoscopic transoral medial pterygomandibular fold approach. (c) The ascending palatine artery was revealed in the prestyloid space. (d) After removing the prestyloid fat in the prestyloid space, the superior pharyngeal constrictor muscle was retracted medially to expose the stylopharyngeus muscle and retropharyngeal lymph node. (e) The ascending pharyngeal artery was between the ICA and retropharyngeal lymph node. It was also revealed after opening the carotid sheath. (f) The retropharyngeal lymph node was completely removed. The dotted oval shows the surgical field after resection of the retropharyngeal lymph node. (g & h) Post-operative enhanced MRI showed the retropharyngeal lymph node was resected completely. (g) Axial MRI plane showed the surgical cavity, longus capitis muscle and ICA. (h) Coronal MRI plane showed the surgical cavity between longus capitis muscle and ICA. APA = ascending palatine artery; APhA = ascending pharyngeal artery; BS = brain spatula; ICA = internal carotid artery; LCM = longus capitis muscle; MPM = medial pterygoid muscle; PF = prestyloid fat; RPLN = retropharyngeal lymph node; SC = surgical cavity; SPCM = superior pharyngeal constrictor muscle; SPM = stylopharyngeal muscle

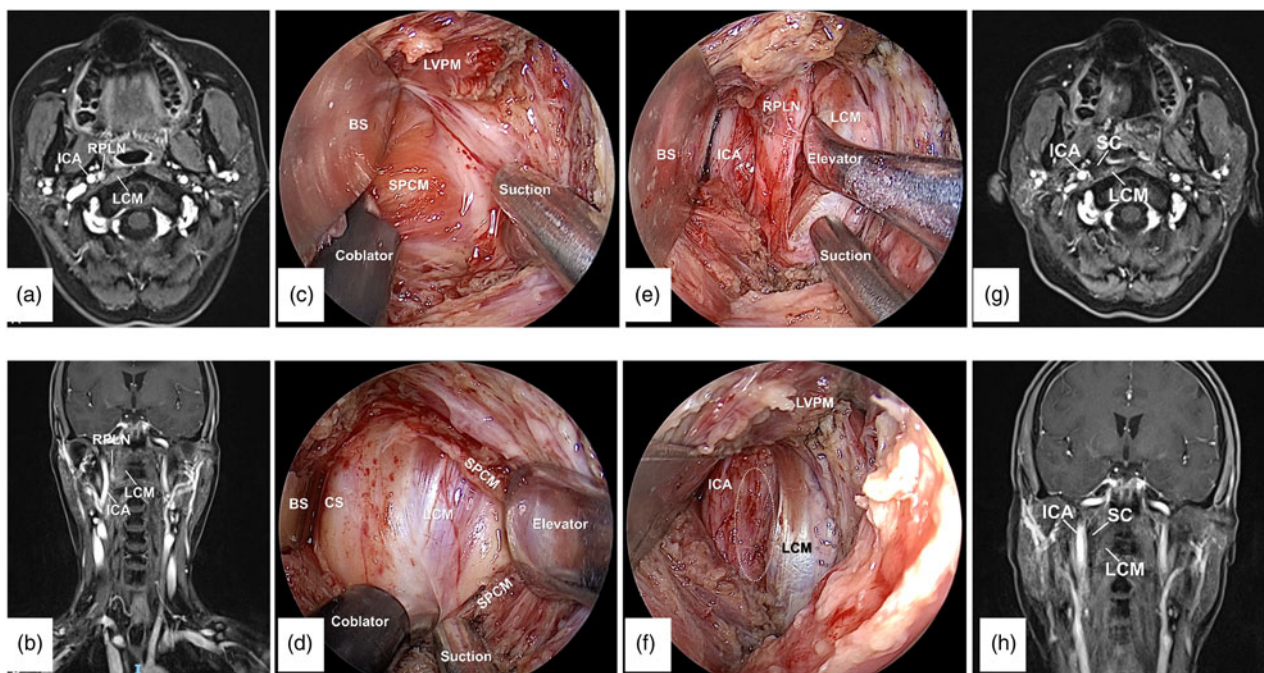
mainly because it is very challenging. The retropharyngeal lymph nodes were occasionally dissected in continuity with the resection of the primary tumour by a partial or total pharyngectomy or a mandibulotomy, such as oropharyngeal and hypopharynx malignancies.<sup>13,23,24</sup> There is currently no safe, minimally invasive or efficient way to resect retropharyngeal lymph nodes, and no way to avoid significant post-operative complications, regardless of whether procedures are open or robotic.<sup>9,10,25</sup>

This study introduced a novel approach for retropharyngeal lymphadenectomy: the endoscopic transoral medial pterygomandibular fold approach. To our knowledge, the endoscopic transoral approach for retropharyngeal lymph nodes recurrence in NPC has not been reported previously. This approach was performed via the prestyloid space, a natural anatomical space exclusively containing fat tissues.<sup>26</sup> Therefore, no bones or other significant structures need to be removed using this approach. The primary surgical technique used in this approach was accurate dissection. The transoral approach provides adequate surgical space for instruments, reduces the risk of injury to vital structures, and causes minimal functional and cosmetic impairments.<sup>27</sup> The endoscopic transoral medial pterygomandibular fold approach is nearly vertical to the coronal plane, and can expose both the retropharyngeal lymph node and ICA in the same surgical field. Complete dissection and en bloc resection of retropharyngeal lymph nodes can be achieved, which is challenging for traditional approaches.<sup>28</sup>

Accurate localisation of retropharyngeal lymph nodes and protection of the ICA are two main aspects of retropharyngeal lymphadenectomy.<sup>28</sup> There are only a few reports on methods

of intra-operative localisation of retropharyngeal lymph nodes. The present study showed that the stylopharyngeal muscle, longus capitis muscle and ICA could be used as landmarks to locate retropharyngeal lymph nodes. Retropharyngeal lymph nodes have been reported to be posterior to the stylopharyngeal muscle, and the stylopharyngeal muscle is the most vertical and medial of the three styloid muscles.<sup>14,29</sup> Our results revealed that dissection posteriorly along the lateral surface of the superior pharyngeal constrictor muscle could reveal the longus capitis muscle. In the surgery, the retropharyngeal lymph node was located anterolaterally to the longus capitis muscle, which served as a reliable landmark to identify the medial margin of the retropharyngeal lymph node. Laterally, the retropharyngeal lymph node was adjacent to the ICA, which was used as a landmark for locating the lateral margin of the retropharyngeal lymph node.

Comprehensive assessment of the ICA was crucial to protect it during surgery, as it is usually adhered to the retropharyngeal lymph node because of radiation, and might be impaired during the procedure. Therefore, it was dangerous to manipulate the ICA rashly without pre-operative evaluation, especially in patients who received re-irradiation.<sup>30,31</sup> Magnetic resonance angiography before surgery was an efficient method for assessing the morphological variations and stenosis of ICA. The balloon occlusion test of the involved ICA with neuromonitoring could evaluate cerebral ischaemic tolerance and reliance on the ICA.<sup>32</sup> When the test result was negative, the balloon guiding catheter was reserved and vessel embolisation was prepared in case of an ICA blowout. Before surgery, the extracranial–intracranial vascular bypass was considered, to



**Figure 4.** Pre-operative imaging, surgical procedures and post-operative imaging examinations of case six. (a & b) Pre-operative enhanced magnetic resonance imaging (MRI) showed an enlarged right retropharyngeal lymph node located between the longus capitis muscle and the internal carotid artery (ICA). (a) Axial plane. (b) Coronal plane. (c–f) Right retropharyngeal lymphadenectomy via an endoscopic transoral medial pterygomandibular fold approach. (c) The levator veli palatini muscle and superior pharyngeal constrictor muscle were exposed. (d) The carotid sheath and longus capitis muscle were exposed. (e) The ICA was exposed, and the retropharyngeal lymph node was identified medial to the ICA. (f) The retropharyngeal lymph node was dissected. The dotted oval shows the surgical field after resection of the retropharyngeal lymph node. (g & h) Post-operative enhanced MRI showed the retropharyngeal lymph node was resected completely. (g) Axial MRI plane showed the surgical cavity, longus capitis muscle and ICA. (h) Coronal MRI plane showed the surgical cavity between the longus capitis muscle and ICA. BS = brain spatula; CS = carotid sheath; ICA = internal carotid artery; LCM = longus capitis muscle; LVPM = levator veli palatini muscle; RPLN = retropharyngeal lymph node; SC = surgical cavity; SPCM = superior pharyngeal constrictor muscle

maintain cerebral perfusion pressure if the balloon occlusion test result was positive and the ICA needed to be resected.

In order to avoid fatal bleeding during surgery, it was also critically important to locate exactly the parapharyngeal segment of the ICA. Several morphological variations of the parapharyngeal segment of the ICA have been reported, including straightness, tortuosity, kinking and coiling.<sup>33,34</sup> Given the lack of constant landmarks, it was quite challenging to locate the parapharyngeal segment of the ICA.<sup>33</sup> The present study showed that a few landmarks could be used to identify the parapharyngeal segment of the ICA: the stylopharyngeal muscle, levator veli palatini muscle and retropharyngeal lymph node. The stylopharyngeal muscle was anterior to the carotid sheath and was a reliable landmark for locating the lower part of the parapharyngeal segment of the ICA, which is consistent with a previous publication.<sup>35</sup> The external orifice of carotid canal was posterior to the attachment site of the levator veli palatini muscle on the inferior surface of the petrosal pyramid, which was a helpful landmark for the parapharyngeal segment of the ICA. As the retropharyngeal lymph node was adjacent to the medial surface of the parapharyngeal segment of the ICA, the enlarged retropharyngeal lymph node itself could be used as a landmark for the parapharyngeal segment of the ICA. During surgery, an ultrasonic Doppler system can also be recommended, to localise the ICA accurately.

The current study demonstrated that the endoscopic transoral medial pterygomandibular fold approach for retropharyngeal lymphadenectomy had a mild effect on the patient's quality of life. No significant post-operative complications were observed. Horner syndrome and effusion in the operative cavity are usually treatable with conservative measures. Horner syndrome has no clear explanation, although stretching of the sympathetic nerve and thermal injuries to the sympathetic

nerve of the neck have been speculated. The leading cause of excess effusion in case one was likely due to suturing techniques associated with inexperience with this approach in this first procedure. The wound was stitched with a multi-layer and mucosal mattress suture style without dead space in the cases that followed. Once the suturing techniques had improved, operative drainage was not required. The nasogastric tube could be retained for two weeks to enhance wound healing. None of the patients required a tracheostomy.

- It is challenging to resect masses in the retropharyngeal space given its anatomical complexity and proximity to the internal carotid artery
- Retropharyngeal lymphadenectomy for recurrent or residual retropharyngeal lymph nodes in nasopharyngeal carcinoma (NPC) is difficult because of the local reaction after radiation
- An endoscopic transoral medial pterygomandibular fold approach to salvage retropharyngeal lymphadenectomy in NPC is safe and efficient

The endoscopic transoral medial pterygomandibular fold approach provides shorter access to the retropharyngeal space than the transcervical approach. This approach is less invasive, and the associated morbidity is less significant than with other approaches. Despite the limited number of clinical cases, with short follow-up durations, the early results from our study are reassuring. Future studies should be conducted to confirm the reproducibility and long-term effectiveness of this surgery. We also realise that surgery is not the only treatment available to these patients. Other therapeutic options available include: radiotherapy, chemotherapy, immunotherapy, targeted therapy and combined treatment. Treatment should be comprehensive and personalised according to the clinical characteristics and the patient's preferences. Surgery was decided by a multidisciplinary team for all patients in our series.

There was a multidisciplinary approach to patient treatment if needed (data are not published here).

## Conclusion

There are challenges associated with retropharyngeal lymphadenectomy using traditional approaches. The endoscopic transoral medial pterygomandibular fold approach is safe and efficient for retropharyngeal lymphadenectomy.

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