DYNAMIC MANUSCRIPT





Prevertebral cervical approach to posterior mediastinum parathyroid adenomas

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Abstract

Background About 4 years ago, we described the pure endoscopic cervical approach to posterior mediastinum parathyroid adenomas, which we called the "prevertebral cervical approach". At that time, we had operated on three patients and did not have enough quality videos to demonstrate this approach. After broadening our experience, we present our results and show this technique through a video.

Methods From June 2015 to January 2021, information on patients undergoing the prevertebral cervical approach was obtained from a specific prospective database, including clinical presentation, biochemistry, preoperative imaging, surgical approach and patient outcomes. The step by step technique is described for both right- and left-sided adenomas, by means of a short video clip.

Results Ten patients were operated on using this technique. Seven adenomas were right-sided and three were left-sided. The mean surgical time was 33 ± 7 min. There were neither intraoperative nor major postoperative complications. Seven patients presented with a slight subcutaneous emphysema, which did not cause complaints. All patients were discharged the day after surgery, except for one patient with a previous open neck removal of four glands due to secondary hyperparathyroidism, which required calcium replacement. Calcium and parathyroid hormone levels were normalised in the other nine patients after surgery. One patient experienced a transient recurrent laryngeal nerve injury which was spontaneously resolved within 1 month. No permanent recurrent laryngeal nerve injury was found. The postoperative cosmetic outcomes were excellent. Conclusion In our experience, the pure cervical endoscopic approach has shown a high feasibility and short operation time, with excellent postoperative results regarding patient comfort, length of stay and disease cure. This approach also offers a very reasonable procedure cost, and may result in a less aggressive surgical option when compared with thoracic approaches.



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Graphical Abstract

Prevertebral cervical approach to posterior mediastinum parathyroid adenomas Posterior mediastinum parathyroid INTERVENTION **OUTCOMES** adenomas (N = 10)SHORT SURGERY DURATION 33.8 min Upper limit SHORT LENGTH OF STAY clavicle 1.2 days Lower limit: LOW COMPLICATIONS RATE Right adenomas (N = 7)**EXCELLENT COSMETIC RESULTS** ALL PATIENT UNDERWENT A PREVERTEBRAL Left adenomas (N = 3) **CERVICAL APPROACH** Rubio Manzanares et al. Surgical Endoscopy 2022 Springer

 $\textbf{Keywords} \ \ \text{Prevertebral cervical approach} \cdot \text{Mediastinum adenomas} \cdot \text{Endoscopic parathyroidectomy} \cdot \text{Parathyroid gland ectopia}$

Parathyroid gland mediastinal ectopia is an unusual but challenging condition in the surgical management of hyperparathyroidism. A mediastinal parathyroid is defined as a gland found completely below the level of the clavicle. Larger series dealing with mediastinal parathyroidectomies show that approximately 60–80% of the ectopic mediastinal parathyroid glands reside in the thymus or anterior mediastinum [1–5], whilst just a few mediastinal glands are located in the middle and posterior mediastinum in variable proportions [6]. Posterior mediastinal parathyroid glands are believed to result from inferoposterior migration of the superior parathyroid glands and can be a rare cause of ectopic parathyroid tissue [7].

Most posterior mediastinum parathyroid ectopia can be removed using an open cervical approach. However, a large incision and an extensive dissection are usually required, and if this approach is not possible, a median sternotomy or thoracotomy is required, which is associated with increased postoperative pain, a prolonged hospital stay and complications in up to 21% of patients [8]. This occurs especially in obese patients or in cases with previous neck surgery.

In recent years, improvements in the imaging test, which have allowed more precise localisation of mediastinal adenomas, along with the development of minimally invasive surgery, have resulted in the development of different endoscopic approaches [8–13].

Transcervical endoscopic or video-assisted approaches always refer to anterior mediastinum adenomas. When focussing on posterior mediastinum adenomas, the proposed techniques are mostly transthoracic, with either an open incision or by minimally invasive video-assisted thoracoscopy [8, 9, 14].

For this reason, in 2017, we developed this technique: a prevertebral cervical approach for posterior adenomas [13]. The cervical approach is a more familiar surgical field for general endocrine surgeons. This approach is likely to result in a less aggressive surgical option when compared with thoracic approaches, due to the lack of pleural incisions. Besides, the cervical approach could lead to easier patient management for anaesthesiologists, as selective bronchial intubation is not needed.

The aim of this study is to present the results of our experience and show how the technique is performed using video clips.



Materials and methods

This paper presents a retrospective study on a prospective database that includes patients diagnosed with hyperparathyroidism who underwent a prevertebral cervical approach between June 2015 and January 2021 at our institution. Patients gave written consent both for surgery and the endoscopic approach. The study was approved by the Ethics Committee for clinical research at the Virgen del Rocio University Hospital (Seville, Spain).

We selected patients who met the following criteria: Adenomas localised in the posterior mediastinum in the imaging test, and adenomas that are found completely below the level of the clavicle (upper limit of the dissection) to D5 level (lower limit of the dissection), regardless of size.

Data collected included demographics, preoperative biochemistry and imaging, and the number of previous parathyroid operations. Operative techniques, findings and duration of surgery were documented, as was the postoperative course, including biochemistry, length of hospital stay, analgesic requirements, histopathology and complications.

All patients were discussed by a multidisciplinary team including a radiologist, endocrinologist and endocrine surgeon before listing for surgery. The surgical intervention was performed under general anaesthesia and tracheal intubation. Antibiotic and antithrombotic prophylaxis was used in all patients. All operations were performed by the same consultant endocrine surgeon. The technique is described in the video step by step. The technique was performed as described in previous work [13].

A three-port prevertebral cervical approach was used, with an 11-mm blunt port for the camera and specimen retrieval, and two 5-mm working ports. Trocar placement in the neck through a 12-mm transversal skin incision on the anterior border of the sternocleidomastoid muscle (SCM) was similar to the technique described by Henry et al. [15], but after a blunt dissection, more distally, and the trocar was placed directly over the prevertebral fascia. Insufflation with carbon dioxide was set at 6-8 mmHg. As recommended in cases with unequivocal localisation in image studies, intraoperative PTH is not needed. No drains were placed at the end of the procedure. All patients had adjusted serum calcium and PTH levels measured on the following morning. Patients were discharged once their pain was controlled satisfactorily with oral analgesia. All patients received at least one follow-up appointment approximately 4 weeks after surgery.

Statistical analyses were carried out using SPSS® for Windows version 21.0 (SPSS Inc., Chicago, IL, United States). Quantitative variables are presented as the mean ± SE and qualitative variables are expressed as frequencies and percentages.

Results

Ten patients underwent prevertebral cervical parathyroidectomy between June 2015 and January 2021 (Table 1). Their mean age was 60 ± 8 (range of 49–74) years, and seven patients were women. The mean body mass index (BMI) was 30.3 ± 6.9 (range of 20.8-44.4) kg/m². All had sporadic primary hyperparathyroidism (PHPT), except one case of secondary hyperparathyroidism (SHPT) who had been operated on previously with a total thyroidectomy for multinodular goitre and supposed total parathyroidectomy without auto-transplantation for secondary hyperparathyroidism at another institution. No more patient was re-operative parathyroidectomy. The rest of the mediastinal parathyroid adenomas were diagnosed before the first parathyroid surgery (n=9). All patients underwent ultrasound imaging, which was negative in all cases. In three cases, Tc-99 scintigraphy was suggestive of mediastinal adenoma. All patients were diagnosed correctly by Tc-99 m-MIBI dual-phase scintigraphy with SPECT/CT, demonstrating in all cases single gland disease on the right or left side of the posterior mediastinum, at the D2–D5 vertebral level (Table 1).

The abnormal parathyroid tissue was at D2 level in two patients, D3 in six patients, D4 in one patient and D4/D5 in another. A left-sided approach was used in three patients, and a right-sided approach was used in seven patients. The mean duration of surgery was 33 ± 6.8 (range of 24–45) min (Table 2). No significant difference was found in surgical time, depending on BMI, or the weight or level of the adenoma. No patients required conversion to another approach. No intraoperative adverse events occurred, either related to pneumomediastinum or due to the surgical technique. All patients returned to the surgical ward after a period of observation in recovery, and no patient required highdependency level care. Seven patients presented with a slight subcutaneous emphysema, which did not cause complaints. One patient required intravenous calcium for postoperative hypoparathyroidism. One patient experienced a transient recurrent laryngeal nerve injury which was spontaneously resolved within 1 month. No permanent recurrent laryngeal nerve injury was found. No infection or postoperative hematoma was found. The mean length of stay was 1 ± 0.6 (range of 1-3) days, and all patients were discharged with oral analgesia only. There were no readmissions within 30 days.

Serum calcium level returned to normal range in all patients, except for one patient with permanent hypoparathyroidism due to a total parathyroidectomy. The serum parathyroid hormone level at first postoperative day was 24.1 ± 16.9 pg/mL (range of 7–59). The postoperative cosmetic outcomes were excellent.

All specimens were reported as parathyroid adenomas. Specimen weights varied between 1.4 and 5.6 g. Posterior



Table 1 Overview of patient demographics, preoperative blood tests and imaging studies

	E										
	IOIAL	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9	Patient 10
Age (years) Median±. SD	60.3 ± 8.3	49	56	69	74	64	61	58	89	54	50
Sex (female/male), (%)	70%/30%	Female	Female	Female	Male	Female	Male	Female	Male	Female	Female
Diagnosis, (%)	PHPT 90%, SHPT 10%	PHPT	PHPT	SHPT	PHPT	PHPT	PHPT	PHPTP	PHPTP	PHPT	PHPT
BMI (kg/m^2) Median \pm SD	30.3 ± 6.9	29.7	28.3	20.8	4.4	38.6	31.9	26.1	26.2	25.0	32.0
No. of previous operations, (%)	None 90% One 10%	0	0	1	0	0	0	0	0	0	0
PTH (pg/ml) Median \pm SD											
Preoperative	123.1 ± 62.4	96	128	229	96	195	87	98	117	159.3	153.2
Postoperative	24.1 ± 16.9	12	17	7	12	18	18	25	23	49.7	59
Neck ultrasound	All negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative
Tc-99 scintigraphy	3 cases	Negative	Negative	Negative	Suggestive	Negative	Negative	Negative	Suggestive	Suggestive	Negative
MIBI-SPECT/CT	All positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive
Parathyroid location											
Side (right/left) (%)	70%/30%	Right	Right	Right	Left	Left	Right	Right	Right	Right	Left
Vertebral level (D2/D3/D4–D5) (%)	20%/60%/20%	D3	D4	D3	D4/D5	D3.	D3	D3	D2	D2	D3

PHPT primary hyperparathyroidism, SHPT secondary hyperparathyroidism, HPT hyperparathyroidism, PTH parathyroid hormone, MIBI-SPECT/CT sestamibi/single-photon emission CT



 Table 2
 Operative outcomes

	TOTAL	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 3 Patient 4 Patient 5 Patient 6 Patient 7 Patient 8 Patient 9	Patient 8	Patient 9	Patient 10
Duration of surgery (min) Median±SD Complication	33.8±6.8	30	32	25	38	36	24	33	32	45	43
Hypocalcaemia	1 hypocalcaemia	No	Hypocalcaemia	No	No	No	No	No	No	No	No
Permanent Recurrent laryngeal nerve injury 0 RLN injuries	0 RLN injuries	No	No	No	No	No	No	No	No	No	No
Haemorrhage	0 Haemorrhage	No	No	No	No	No	No	No	No	No	No
Length of stay (days) Median±SD	1.2 ± 0.6	1	1	3	1	1	1		1	1	1
Histology	All adenomas	Adenoma	Adenoma	Adenoma	Adenoma	Adenoma	Adenoma	Adenoma	Adenoma	Adenoma	Adenoma
Weight of parathyroid gland (g) Median \pm SD 3.8 \pm 1.2	3.8 ± 1.2	2.6	2.9	3.7	5	4.6	3.7	5.6	4.4	1.4	4.2

revisions confirmed a satisfactory evolution and the cure of the disease (Table 2).

Discussion

The key to successful surgical excision of an ectopic mediastinal parathyroid adenoma is accurate preoperative localisation. Specialised imaging studies aid in the localisation of a target for surgical resection [8].

Ultrasound imaging of the neck is usually the first line imaging study. However, ultrasonography is unlikely to identify an ectopic mediastinal parathyroid adenoma [8, 16]. In our experience, the combination of scintigraphy and CT scans provide the best accuracy for localising mediastinal parathyroid glands. Similar to other authors, [11] we found the information provided by sestamibi scintigraphy to be complementary to that obtained from CT images, and patients required a positive anatomic imaging study in addition to scintigraphy prior to surgery. In fact, in three patients, a scintigraphy was performed where a mediastinal adenoma was suggested. However, a more specific imaging study was necessary to determine the precise location. Technetium-99 m-radiolabelled methoxyisobutylisonitrile (MIBI), which can be combined with single-photon emission CT (SPECT) and low-dose CT, combines functional and anatomical imaging of parathyroid adenomas, with a sensitivity approaching 97% [8]. In this way, in our series, Tc-99 m-MIBI dual-phase scintigraphy with SPECT/CT was performed in all patients with a positive result. This strategy enabled us to avoid a negative neck exploration.

Once the ectopic adenoma has been located, the main question lies in the selection of the approach method. Most ectopic glands are found in the superior mediastinum in the thymus gland and can be excised via a cervical incision. However, parathyroid adenomas found deeper in the mediastinum remain a challenge [8], especially those found in the posterior mediastinum. Although cervicotomy presents a more familiar exposure to the endocrine surgeon, the location deep in the posterior mediastinum puts this approach out of reach of the parathyroid glands located in the posterior mediastinum. For this reason, it has traditionally been necessary to add a sternotomy or a thoracotomy to the cervicotomy to access them, requiring large dissection no exempt from complications [8, 11].

Median sternotomy or thoracotomy have been the traditional approaches to excision of mediastinal parathyroid adenomas. Nevertheless, median sternotomy and thoracotomy remain invasive procedures requiring a significant hospital stay [11]. Furthermore, the complications of these approaches, though occurring at a rate of less than 3%, may be devastating [11]. Therefore, several less invasive approaches for mediastinal parathyroid lesions are



advisable. In this way, the prevertebral cervical approach for posterior mediastinal adenomas could be an option to consider. None of the patients in our study required thoracotomy for parathyroid excision and nine of ten patients were discharged 24 h after surgery without any complications. All posterior prevertebral approach patients were discharged home by the third postoperative day.

In recent years, the transoral endoscopic parathyroidectomy vestibular approach (TOEPVA) has emerged as an alternative in the parathyroid and thyroid surgery [17]. It is a technique in development with contradictory results in the literature [18, 19]. This technique may be an option in well-localised orthotopic adenomas and in very well selected cases of ectopic parathyroid adenomas located in the upper anterior mediastinum in patients with a special cosmetic concern [17]. However, for those adenomas located in the posterior mediastinum, in our opinion, dissection would be difficult due to the placement of the trocars, limiting access to the posterior mediastinum and, in the unlikely case of being accessible, they would require extensive dissections and long surgical times. In contrast, the prevertebral cervical approach for posterior mediastinal adenomas could be a more straight-forward and familiar exposure for endocrine surgeons avoiding large dissections and offering cosmetic results similar to TOE-PVA technique.

An attractive approach for appropriately selected patients is video-assisted thoracoscopic surgery (VATS). This technique was described by Pritz et al. in 1994 [20], with the literature suggesting a shorter hospital stay and lower complication rates [8, 14, 21]. The overall success rate was reported as up to 98–100% [10, 22]. Nevertheless, the success of thoracoscopy is dependent on accurate preoperative localisation, which helps determine which side of the chest to access. There are limited published data on VATS parathyroidectomy, and it is recommended that the procedure should be performed only in specialised units with a multidisciplinary team [8]. In spite of the good results reported with VATS techniques, they have not been widely used, probably due to their more recent development, lack of wide availability and higher costs [23–25]. Besides, these techniques have the issue of longer operative times, usually over 1.5 h.

Many questions still remain in terms of the optimal management of mediastinal adenomas. Whilst most mediastinal parathyroid adenomas can be resected via a cervical incision, this is not possible in 1–2% of cases [22]. The difficulty lies in determining the best approach for each patient. Iihara et al. [26] suggested the level of the aortic arch on the horizontal chest CT should be used as a landmark for choosing a suitable surgical approach. Adenomas found above the aortic arch in the superior mediastinum

can be treated successfully using a transcervical approach, whilst those found in the middle or posterior mediastinum below the level of the aortic arch should be approached transthoracically [20, 22].

In our experience, there should be one more subdivision. Posterior adenomas located between the aortic arch or clavicular level and the D4–D5 vertebral level can benefit from a prevertebral cervical approach. This approach offers certain advantages over the transthoracic approach; it does not require selective intubation of the lung and is also a field that endocrine head and neck surgeons are acquainted with. This is further supported by our data, in which the mean surgical time was 33 min, a significantly shorter surgical time than for VATS.

On the other hand, thoracoscopy requires the incision of the pleura in order to remove the ectopic tissue, which may be more painful and can require the use of drains more frequently.

The prevertebral cervical approach may be limited by the size of the adenoma. Deep adenomas less than 1 cm may be very hard to find and may not be suitable for this approach. On the other hand, due to the narrow surgical field, adenomas larger than 4 cm in transverse diameter may be very difficult to handle. In both cases, VATS may be the best option for these patients.

In conclusion, the prevertebral cervical approach is a feasible, safe technique associated with few postoperative complications and an excellent cosmetic outcome. Accurate, unequivocal preoperative localisation of the enlarged parathyroid gland using an MIBI-SPECT/CT scan is essential. In our experience, the prevertebral cervical approach may be an alternative to VATS for selected patients with hyperfunctioning parathyroid glands in the upper posterior mediastinum.

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Declarations

Disclosures Juan Manuel Martos Martínez and Javier Padillo Ruiz have promoted and developed the study. Mercedes Rubio-Manzanares Dorado, Juan Manuel Martos Martínez and Verónica Pino Díaz have contributed substantially to the conception and design of the study and acquisition of data. Mercedes Rubio Manzanares Dorado and Verónica Pino Díaz has analysed and interpreted the datas; Mercedes Rubio-Manzanares Dorado has written the manuscript. Javier Padillo Ruíz and Juan Manuel Martos Martínez has revised the manuscript for important content. Javier Padillo Ruíz and Juan Manuel Martos Martínez have participated with a very similar input, it should be stated that those authors contributed equally. Final approval of the version to be published has been given by all authors. Mercedes Rubio Manzanares Dorado, Verónica Pino Diaz, Javier Padillo Ruíz, Juan Manuel Martos Martínez have no conflicts of interest or financial ties to disclose.



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