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Robotic surgery for primary hyperparathyroidism

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Abstract
Background Open cervical parathyroidectomy is the standard of care for the treatment of primary hyperparathyroidism (PHP). However, in patients with a history of keloid or hypertrophic scar formation, the cosmetic result may sometimes be unsatisfactory. Furthermore, in the presence of mediastinal glands, a more morbid approach is sometimes necessary, involving a sternal split or thoracotomy. Robotic parathyroidectomy, either transaxillary or transthoracic, could be an alternative in both settings.
Methods Between 2008 and 2013, 14 patients with PHP and a well-localized single adenoma underwent robotic transaxillary cervical (TAC) ($n = 8$) or transthoracic mediastinal (TTM) ($n = 6$) parathyroidectomy at an academic tertiary medical center and their outcomes were analyzed.
Results All 14 operations were completed successfully as planned. For TAC and TTM parathyroidectomies, mean operative time was 184 and 168 min, respectively. With the exception of one TTM patient, intraoperative PTH determination indicated a >50 % drop in all patients 10 min after excision and no patients presented with recurrent disease on follow-up. Average length of hospital stay was 1 day after TAC parathyroidectomy and 2.2 days after TTM. On a visual analog pain scale (0–10), average pain scores after TAC were 6/10 on postoperative day 1 and 1/10 on day 14, compared to 7.7/10 and 1.5/10, respectively, after TTM. Complications included development of seroma in 1 patient in the TAC group and pericardial and pleural effusion in 1 patient in the TTM cohort.
Conclusions This initial study shows that robotic TAC and TTM parathyroidectomy are feasible in selected PHP patients with preoperatively well-localized disease. Although the TAC approach offers a potential cosmetic benefit in patients with a history of keloid or hypertrophic scar formation, a more generalized use cannot be recommended based on current evidence. The robotic TTM approach presents a minimally invasive alternative to resections previously performed through thoracotomy and sternotomy.

Keywords Parathyroidectomy · Robotic · Mediastinal · Transaxillary · Outcomes

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Since its original description in 1925 by Felix Mandl in Vienna, parathyroidectomy has been traditionally done through a neck incision, with minimal morbidity and a greater than 95 % cure rate for primary hyperparathyroidism [1]. Over the last decade, with the advances in preoperative tumor localization and intraoperative intact PTH assays, alternative techniques utilizing a more limited focused dissection have been developed, resulting in smaller incisions [2].

Since the neck is a critical part of the body for cosmesis, there have been attempts to perform parathyroidectomy

through alternative, potentially more cosmetically acceptable, incisions since the beginning of the laparo-endoscopic era in the 1990s. In fact, the first "minimally invasive" video-assisted parathyroidectomy was described by Gagner et al. in 1996, though this method did not gain widespread acceptance due to difficulties with exposure and poor perioperative outcomes associated with CO_2 insufflation [3]. Subsequent video-assisted techniques introduced by Miccoli using a hybrid approach have received more popularity, with minimization of the cervical incision scar [4–6].

Nevertheless, these alternative approaches have not been able to reach the ultimate goal of neck scar elimination and maximum cosmetic benefit that could be offered by performing the operation through remote incisions. Although cervical incisions become incorporated to the Langer lines and are not a source of concern to most patients, this is not the case in the subgroup of patients with a history of hypertrophic scar (HS) or keloid formation, since in this population even minimal incisions may result in disfiguring scars.

A second population where the surgical management of PHP becomes more challenging and complex includes patients with parathyroid disease in the mediastinum. Parathyroidectomy in these patients often involves a sternotomy or thoracotomy and is associated with increased morbidity. A minimally invasive approach could, therefore, offer a significant benefit by accelerating patient recovery, decreasing pain, and minimizing morbidity for these patients [7].

In both populations, prior experience suggests that a robotic approach could help overcome these issues. In a similar context, transaxillary cervical (TAC) thyroidectomy has been successfully performed through remote incisions [8]. Furthermore, robotic transthoracic mediastinal (TTM) surgery has been well established for thymectomies [9, 10]. While video-assisted thoracic approaches have been also been described [11], it was anticipated that the improved visualization provided with robotic optics and the increased freedom of motion of the robotic arms and graspers could provide advantages in mediastinal parathyroid resection. A robotic endocrine surgery program was established at our institution in 2008, and techniques for robotic thyroidectomy and adrenalectomy have been previously described [12–14]. The aim of this study is to describe the technique and assess the safety and feasibility of TAC and TTM robotic parathyroidectomy in a selected group of patients with PHP.

Materials and methods

Between 2008 and 2013, 14 patients with PHP underwent robotic TAC ($n = 8$) or TTM ($n = 6$) parathyroidectomy.

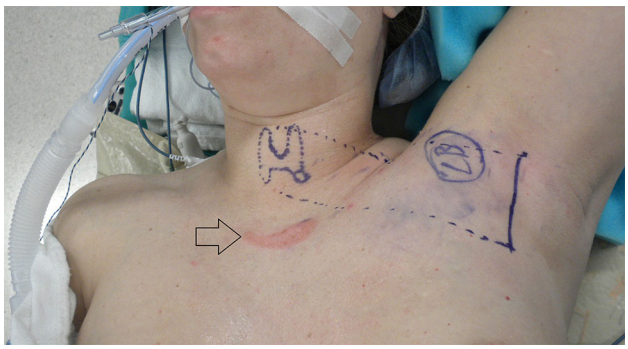

Fig. 1 Patient positioning and the surgical planning for a robotic transaxillary cervical parathyroidectomy. Note the keloid formation on the chest from an old abrasion (*arrow*), which was the main motivation for the patient to consider robotic parathyroidectomy

Patients were candidates for robotic TAC parathyroidectomy if they had a thin body habitus (BMI < 30), no history of prior neck surgery, a single abnormal gland was identified on preoperative ultrasound and/or sestamibi scan, and they did not want the procedure performed through a neck incision. An extensive preoperative discussion was held with the patients regarding the limitations of a focal or unilateral exploration for PHP according to currently available data in the literature [15–17]. Informed consent was obtained. Surgical technique was similar to previous reports of robotic TAC thyroidectomy by the same group [12]. In brief, the patient is placed supine on the operating room table and general anesthesia is administered. Preoperative antibiotic prophylaxis is administered. The neck is hyperextended using a bean bag. The upper extremity ipsilateral to the localized parathyroid gland is placed on an arm board at 90° flexion around the elbow and shoulder joints (Fig. 1). The contralateral arm is tucked along the side of the patient. Then, preoperative neck ultrasound is performed to identify the suspected parathyroid adenoma. The skin projections of the thyroid and parathyroid are marked to guide the subcutaneous flap, which is created after a 5–6-cm incision is made along the ipsilateral axilla, lateral to the lateral edge of the pectoralis major muscle. After the two heads of the sternocleidomastoid muscle are identified, an elevating Chung retractor is placed and the thyroid is exposed. The robot (da Vinci S/Si, Intuitive Surgical, Sunnyvale, CA) is subsequently docked, coming in from the contralateral shoulder (Fig. 2). The procedure is performed using the robotic 10-mm down-viewing 30° scope, Harmonic scalpel (Ethicon Endo-Surgery, Cincinnati, OH), and Cadiere forceps. Initially, the thyroid is identified and dissection is guided by the preoperative ultrasound. The parathyroid adenoma is then identified and resected (Fig. 3). Intraoperative PTH levels are drawn pre-excision and at 10 min post-excision by the anesthesia

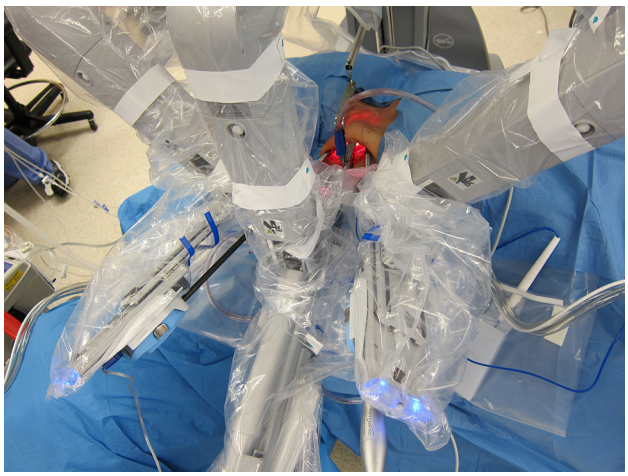

Fig. 2 Docking of the DaVinci robot for robotic transaxillary cervical parathyroidectomy. A 2-arm approach was used with a 30° down-viewing robotic camera

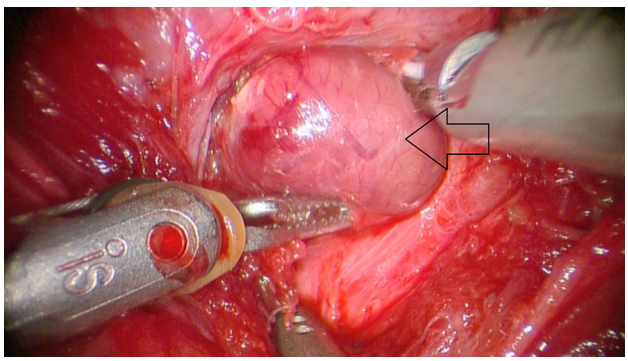

Fig. 3 Dissection of a left-lower parathyroid adenoma (*arrow*) through a transaxillary cervical approach

team through peripheral veins. A drop in PTH level by 50 % is considered to be consistent with a successful resection. In cases where the exposure is appropriate, unilateral exploration is completed by dissecting the 2nd parathyroid gland on that side, while waiting for the PTH results. The operative site is then irrigated, and hemostasis was checked. The robot is undocked and the incision is closed in the standard fashion.

Patients were candidates for robotic TTM parathyroidectomy if they presented with sestamibi scan uptake in the mediastinum (typically anterior) and no evidence of disease in the neck on sestamibi scan or ultrasound. In general, previous chest surgery was considered a contraindication to the robotic approach. Intraoperative PTH guided explorations in all patients. The standard approach to robotic resection of mediastinal parathyroids is a right-sided, 3-port, unilateral technique. Careful preoperative localization of the tumor prior to surgery is critical for a successful outcome.

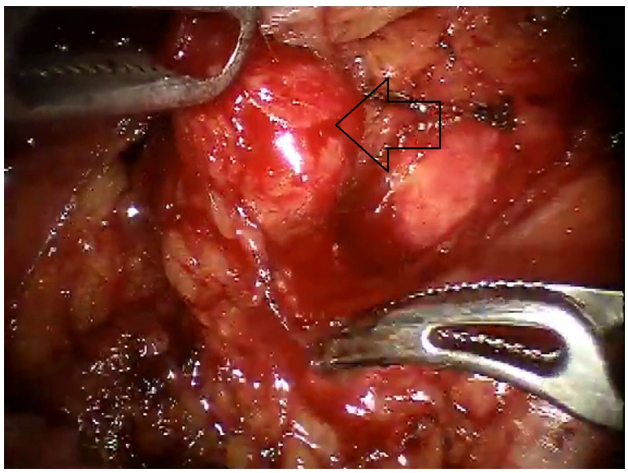

Fig. 4 Parathyroid adenoma (*arrow*) embedded in the aortopulmonary window, between the phrenic nerve and the vagus nerve, exposed during a transthoracic mediastinal robotic parathyroidectomy

Multiple approaches have been described for resection of mediastinal tumors with some surgeons preferring a right-sided approach and others preferring the left [18]. We typically prefer the right-sided approach given that the left ventricle and heart occupy a significant portion of the left hemithorax, making placement and maneuvering of the robotic arms more difficult. The patient is intubated with a double-lumen endotracheal tube and placed in the lateral decubitus position with the right arm gently tucked posteriorly and the hemithorax elevated to 30° with a folded blanket beneath the hips and chest. Lung isolation is initiated, and a transpleural approach is taken. The camera is centered in the hemithorax at approximately the 6th interspace, mid-axillary line, and directed to the mediastinum. Under direct visualization, the left-sided robotic arm is placed in the 2nd interspace and the right-sided arm in the 7th interspace, both in the anterior axillary line. Due to the very small size of the tumors and difficulty differentiating mediastinal fat from parathyroid adenoma, a full thymectomy, with en bloc resection of mediastinal fat, is carried out to assure that the tumor has been resected. Borders of the resection are the diaphragm caudally, the thyroid gland cranially, and the phrenic nerves laterally, all of which are dissected meticulously (Fig. 4). To confirm that the tumor has been resected, a rapid serum PTH level is sent prior to removal of the thymus gland and then 10 min after removal. A drop in PTH level by 50 % is considered to be consistent with a successful resection. Additionally, a frozen section of the specimen is performed to confirm that a parathyroid adenoma is present. At the completion of the procedure, the lung is re-inflated and a 20-French chest tube is placed.

In all patients, postoperative pain management included a combination of oral ibuprofen and/or acetaminophen with

supplemental oral breakthrough opioids when required. Pain levels on postoperative day 1 and 14 were measured by nursing staff according to a visual analog scale, ranging between 0 (no pain at all) and 10 (worst pain imaginable). Total serum calcium (Ca), phosphorus (P), and PTH levels were measured on postoperative day 1, 14 and at 6 months. Demographic, clinical, and surgical data were obtained from a prospectively maintained IRB-approved database. Statistical analysis was performed using JMP software version 9.0.0 (SAS, Cary, NC). Values are presented as mean ± standard error of the mean unless otherwise indicated.

Results

In the TAC group ($n = 8$), the mean age was 47.3 ± 12.5 years and all patients except one were female. Four patients had a history of keloid or HS formation in the past. All patients had new-onset PHP. A parathyroid adenoma was visible on preoperative neck US in all patients and on sestamibi in seven patients. The operative approach was focal in three and unilateral in five patients. The mean operative time was 184 ± 58 (range 125–314) minutes, with flap, docking, and console times of 42 ± 19, 12 ± 5, and 58 ± 23 min, respectively. All patients had a single adenoma that was right superior in three, right inferior in two, left superior in two, and left inferior in one patient. The average tumor size was 15.3 ± 5.7 mm (range 8–24 mm). Intraoperative PTH monitoring was used in all patients, and a drop greater than 50 % at 10 min post-excision was documented in the entire cohort (mean drop 82 %, SD 7.5, range 73–94 %). All patients were discharged home on postoperative day (POD) #1. The average pain score on POD #1 was 6.0 ± 2.0, and on POD #14 it was 1.0 ± 2.1. The only complication was a postoperative seroma in one patient that was managed conservatively in the outpatient setting, and no patient manifested evidence of recurrent laryngeal nerve injury or voice symptoms at follow-up. There was no evidence of recurrent disease at a median follow-up of 29 (range 6–38) months. Of note, over the same time period (2008–2013), the option to proceed with TAC parathyroidectomy was offered to an additional three patients who elected to proceed with the traditional (open) cervical approach, while the total number of traditional parathyroidectomies performed at our institution over the same period was approximately 1,500.

In the TTM group, there were four female and two male patients with a mean age of 48.2 ± 16 years. Two patients presented with a new-onset PHP and four with persistent disease. There was no evidence of cervical disease in these patients on US or sestamibi, whereas an increased mediastinal sestamibi uptake was demonstrated in all. Operative time was 168.2 ± 63.6 minutes. Ectopic parathyroid glands were located in the anterior mediastinum in four patients, inferior to the aortic arch in one, and in the pericardium in one patient. A radio-guided approach was used in one patient. Intraoperative PTH drop of greater than 50 % at 10 min post-excision was documented in all but one of the patients (mean drop 74 %, SD 20, range 35–87 %). Pathology confirmed the presence of parathyroid adenomas in all 6 specimens. The average tumor size was 11.8 ± 3.2 mm (range 6–15). The hospital stay was on average 2.2 ± 1.0 days. The mean pain score was 7.7 ± 1.6 on POD #1 and 1.5 ± 3.7 on POD #14. After a median follow-up of 9 (range 1–17) months, no recurrent disease was detected. One patient was readmitted on POD #6 with pericardial and bilateral pleural effusions secondary to Dressler's Syndrome and underwent video-assisted thoracoscopic pericardial window and placement of a pleural drain. He was discharged home in good condition 3 days later and has had complete recovery. There were no conversions to conventional surgery in either the TAC or TTM groups.

Discussion

This study describes the technique and demonstrates the safety and feasibility of robotic TAC and TTM parathyroidectomy in an initial selected group of patients. The comments of the authors regarding the TAC approach mirror those reported previously for robotic transaxillary thyroidectomy [12, 13]. Although the procedures were performed safely from a remote incision, this is a more invasive surgical procedure than the traditional cervical approach due to the extent of surgical dissection and longer operative times. The most difficult part of the procedure was the flap formation, with the actual parathyroid dissection being relatively easier, thanks to the magnified view and the dexterity obtained from articulating instruments. Therefore, a future modification of the robotic technique that utilizes a more limited flap dissection would dramatically enhance this procedure and render it less invasive. Based on these limitations, the indications for this approach appear to be restricted at this point to patients with documented HS or keloid formation and those who remain determined to pursue a scar-less (in the neck) approach, once the potential pitfalls of the robotic approach have been extensively discussed.

The prerequisite for pursuing the robotic TAC technique was the localization of a single gland on ultrasound. With these findings, the intraoperative identification of the adenoma in the neck was uncomplicated. A unilateral approach was possible in 62.5 % of the patients (5 out of 8). However, a significant limitation of this approach was

the inability to perform a bilateral exploration given the inadequate contralateral exposure with current technology, since the use of a bilateral axillary approach would have added unacceptable morbidity for these patients. Therefore, this limitation was discussed very clearly with the patients and it was underscored that if the intraoperative PTH levels did not drop appropriately, they would need a conventional neck exploration. Despite this discussion, all eight patients remained very motivated to have this procedure done through a remote incision.

While case reports have previously indicated that TAC parathyroidectomy is both feasible and safe [19, 20], the only published series is by Tolley et al. [21] reporting the results of 11 patients with primary hyperparathyroidism who underwent robotic TAC parathyroidectomy in 2011. In their cohort, the mean exposure and console times were 31 and 51 min, respectively. Contrary to our selection criteria, they reported a preference for patients with inferior adenomas located further away from the recurrent laryngeal nerve to facilitate a robotic approach. Accordingly, all but one of their patients had inferior parathyroid adenomas. It was the remaining patient with the right superior adenoma that was the only one in the series requiring conversion to open due to suboptimal surgical access secondary to large body habitus. No complications were reported, and all patients were discharged within the first 24 h. In our series, half of our cervical cases ($n = 4$) presented with superior parathyroid adenomas and conversion to open was not needed in any of the patients. The exposure (flap) and console times were similar to this study. We believe that the superior glands can be resected as safely as the lower glands in the hands of surgeons familiar with the recurrent laryngeal nerve anatomy. Nevertheless, respecting the traditional parathyroid surgery principles, the dissection should be performed close to the capsule of the gland, with minimal use of energy.

The robotic approach has more significant advantages in the management of mediastinal adenomas, when compared to the conventional procedures that require a sternotomy or thoracotomy in one-third of the cases. A recent study comparing open to robotic thoracoscopic approaches for the resection of mediastinal masses suggested significant benefits in morbidity and quality of life with the latter [7]. The small amount of data in the literature also suggests that robotic TTM parathyroidectomy can be performed safely with enhanced postoperative recovery compared to open procedures [22, 23]. Our series of six patients further attests to the safety, feasibility, and efficacy of the robotic approach for mediastinal parathyroid adenomas, as well as the decreased morbidity associated with this modality. While video-assisted thoracic surgical (VATS) resection of mediastinal parathyroids is possible without robotic assistance, it is our observation that the robot facilitates the operation and provides enhanced visualization of the mediastinum and improved maneuverability in small working spaces. The occurrence of a complication (pericardial effusion) requiring re-admission and return to the operating room highlights the morbidity of mediastinal surgery, whether robotic or open, and indicates that given the risks involved, the decision to proceed with a mediastinal parathyroidectomy should only be made in the presence of a well-localized gland on preoperative imaging.

In conclusion, this study presents an initial safety and efficacy evaluation of the robotic approaches to PHP. Despite the small sample size, it is the largest combined experience of robotic TAC and TTM parathyroidectomies to our knowledge. With the techniques described, all patients were treated successfully with no evidence of recurrence at follow-up and an acceptably low morbidity. Furthermore, considering the learning curve associated with robotic surgery, there is certainly an opportunity to improve the operative times with increasing experience. At present, the best candidates for robotic parathyroidectomy are PHP patients presenting either with a history of HS/keloid formation and a solitary cervical gland identified on localizing studies or with disease that has been localized to the mediastinum.

Disclosures The authors, Drs. Georgios Karagkounis, Duygu Derya Uzun, David P. Mason, Sudish C. Murthy, and Eren Berber, have no conflicts of interest or financial ties to disclose.

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