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ENDOCRINE SURGERY

Totally endoscopic lateral parathyroidectomy: prospective evaluation of 200 patients

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Abstract
Purpose Several new minimally invasive techniques (mini-open, video-assisted, and endoscopic procedures) for parathyroidectomy have been described. However, totally endoscopic lateral approach parathyroidectomy (Henry technique) is not routinely performed.
Methods This is a prospective study of 200 consecutive patients that underwent totally endoscopic lateral parathyroidectomy.
Results Two hundred of 387 patients (52%) with primary hyperparathyroidism were included. Fifty-six patients (28%) were converted to open parathyroidectomy. Causes for conversion were lack of intraoperative localization (11%), difficult dissection (10%), bleeding (4%), failure of normalization of IOPTH results (2%), and other causes (1%). Gland localization (areas 1 to 2 versus area 3) and CaPTHus score (<3 versus ≥3) were not associated with the risk of conversion. Mean postoperative follow-up was 13 months, and 196 patients (98%) were cured.
Conclusions Totally endoscopic lateral approach can be proposed in more than half of the patients with good immediate results. Conversion rate remains important and may explain low acceptance rate of this technique.

Keywords Hyperparathyroidism · Parathormone · Parathyroidectomy · Endoscopy · Parathyroid · Adenoma

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Introduction

Primary hyperparathyroidism (PHPT) is one of the most common endocrine disorders for which parathyroidectomy is the most effective therapy [1]. Bilateral neck exploration with a collar incision is considered to be the standard surgical approach to parathyroid surgery for PHPT. This procedure has excellent published results, with cure rates of 95–99% and complication rates of 1–3% [2]. However, as around 85% of patients have single gland disease and the majority, therefore, have unnecessary extensive exploration, effort has been focused on minimizing the extent of neck dissection [3, 4]. Unilateral exploration (one side) and then selective or focused parathyroid surgery (one gland) have been proposed since the introduction of improved preoperative localization studies and intraoperative parathyroide hormone monitoring (IOPTH). Focused exploration is currently the standard technique for parathyroidectomy. To date, several different minimally invasive operations have been described, but the three main surgical accesses are the

open mini-incision (OMIP), the video assisted without gas insufflation (VAT), and the totally endoscopic lateral approach with gas insufflation (EP) [4–6]. Retrospective evaluations and a limited number of randomized studies have been performed evaluating these minimally invasive approaches versus bilateral neck exploration [2, 4, 5]. Despite a rapid worldwide acceptance of these minimally invasive approaches in most endocrine surgery centers, the use of an endoscope to perform parathyroidectomy remains controversial [7].

Totally endoscopic lateral approach is not widely performed, and studies from other centers using this technique have rarely been published [4, 5, 7, 8]. Totally endoscopic lateral parathyroidectomy was described by Henry et al. [7, 8] in 1999. We performed a prospective evaluation of 200 consecutive patients that underwent totally endoscopic lateral parathyroidectomy. The aim of this study was to determine the feasibility of this approach, postoperative results, and factors that influence conversions to cervicotomy.

Methods

In 2001, a prospective StatView database (StatView 5.0.1 for Windows; SAS Institute Inc, Cary, NC, USA), a documentation of patients with PHPT was started, recording preoperative and intraoperative parameters. Retrospective review of this prospectively maintained database identified 387 patients that underwent parathyroidectomy between 2001 and 2008. According to our diagnostic algorithm, all patients had ultrasound and sestamibi scintigraphy as preoperative localization studies in the department of nuclear medicine (JC Mayer). Patients with concordant ultrasound and sestamibi identifying one abnormal gland were scheduled for totally endoscopic lateral parathyroidectomy. However, patients were separated in two groups whether or not they had strictly concordant preoperative US and Mibi results. Patients with known hereditary hyperparathyroidism (multiple endocrine neoplasia, familial hyperparathyroidism), radiation-induced hyperparathyroidism, parathyroid cancer, patients undergoing reoperation, concomitant thyroid surgery, and those with discordant ultrasound/sestamibi results were excluded [1].

Age, gender, preoperative total calcium and parathormone levels, ultrasound, and sestamibi findings were evaluated. A dichotomous scoring model, proposed to identify patients with PHPT due to single-gland disease was calculated in all patients [9].This score (CaPTHus score) uses five preoperative variables (total calcium level≥ 3 mmol/L (or 120 mg/L); intact PTH level≥2 times the upper limit of normal levels; positive ultrasound and sestamibi scan results for one enlarged gland; concordant ultrasound and sestamibi scan findings). A score of 3 or higher was estimated to have a positive predictive value of 100% to correctly predict single gland disease [9].

Totally endoscopic lateral parathyroidectomy as described by Henry et al. was performed by two surgeons. A 10-mm incision was made at the anterior border of the sternocleidomastoid muscle and deepened by sharp and blunt dissection to create a space lateral to the ipsilateral thyroid lobe and medial to the carotid artery and the internal jugular vein. Two 3-mm trocars were introduced cranially and caudally to the incision along the anterior sternocleidomastoid muscle border and a 5-mm trocar with a 0° endoscope was placed in the initial incision, which was temporarily closed by a purse-string suture. Carbon dioxide was insufflated at a pressure of 8 mmHg to expand the artificial space, and dissection was performed with 3-mm instruments. During the procedure, identification of the recurrent laryngeal nerve or the ipsilateral parathyroid was not mandatory. In all patients, IOPTH were performed before (pre-incision) and at the time of skin incision, directly before parathyroid excision (pre-excision), and subsequently, 10 and 20 min after parathyroid excision. IOPTH was considered as positive (successful parathyroidectomy) when there was a decrease of more than 50% between either the pre-incision or pre-excision level and 10 min post-excision level [4].

Operation side, operative time, conversions, and causes of conversion were analyzed. After parathyroidectomy, resected pathologic gland locations were classified according Henry classification [7]. Three areas were described: posterior to the two superior thirds of the thyroid lobe (area 1); at the level of or below the inferior pole of the thyroid lobe but in a plane posterior to it (area 2); at the level of or below the tip of the inferior pole of the thyroid lobe but in a superficial and anterior plane (area 3). After parathyroidectomy, nonspecific morbidity was evaluated using Clavien classification [10]. Specific morbidity (recurrent nerve and parathyroid) was evaluated also. Postoperative laryngoscopy was not routinely performed but only in any patient experiencing voice discomfort.

All patients stayed at least overnight in hospital and postoperative serum levels of calcium were recorded on day 1 and again later if needed. Total calcium and PTH levels were determined in all patients at 6 weeks and at 6 and 12 months after parathyroidectomy. Upper limits for calcium and PTH serum levels were defined as <2.62 mmol/L (or 105 mg/L) and <65 pg/mL, respectively. The biochemical cure was correlated with the histology report. Persistent HPT was defined as persistence of elevated total calcium and PTH levels after surgery. Recurrent HPT was defined as increase in calcium and PTH at least after a 6-month period of normocalcemia. The follow-up period was important in providing the cure rate and eliminating persistence and recurrence.

For statistical analyses, all variables were summarized using means and standard deviations. Continuous parametric variables were compared using *t* tests. The Mann–Whitney *U* test was performed for nonparametric variables. Nominal variables were compared using Chi-square analysis and Fisher's exact test when nonparametric. Statistical analysis was performed using commercially available software Statview 5.0.1 (SAS Institute Inc, Berkeley, CA).

Results

Two hundred consecutive patients of 387 (52%) operated for primary hyperparathyroidism at Nancy University Medical Center underwent a totally endoscopic lateral approach and were included in this study. All patients were considered as sporadic HPT1 patients at the time of parathyroidectomy. Eventually, one patient turned out to have a MEN1 mutation that was diagnosed 6 months after parathyroidectomy. Patients mean age was 63.1 years (range 13–87) and the majority of these were female (n= 165; 82%). Mean preoperative calcium and PTH levels were 2.8±0.2 mmol/L (or 112±9 mg/L) and 173±274 pg/mL, respectively. The preoperative calcium and PTH levels were both abnormally elevated in 184 patients (92%). There were 16 patients (8%) that had an unsuppressed PTH with a high normal or elevated calcium. Mean preoperative values for calcium, PTH, and other patients' characteristics were similar between first 100 and last 100 patients (Table 1).

All patients were considered to have one localized enlarged parathyroid gland before undergoing parathyroidectomy using totally endoscopic lateral approach. One hundred and seventy-seven patients (89%) had concordant preoperative sestamibi and ultrasound results (strictly concordance). The remaining 23 patients (11%) were considered to have one localized enlarged gland, but their ultrasound and sestamibi results were not strictly concordant. Thirteen patients (6%) had one enlarged gland localized by ultrasound with negative or equivocal sestamibi results. Seven patients (3%) had one enlarged gland localized by sestamibi scintigraphy but negative US results. Three patients (2%) had both positive and equivocal ultrasound and sestamibi results. CaPTHus score was ≥3 in 177 patients (88%) and was <3 in 23 patients (12%). Parathyroidectomy using totally endoscopic lateral approach was performed in 92 patients (46%) on the right side and in 108 patients (54%) on the left side (Table 1).

Mean operative time was 71±26 min (14–170 min) in all patients and was 8 min shorter in the last 100 patients (p=0.04; Table 1). According to data from surgical exploration (Henry classification), 51 patients had an adenoma in localization area 1 (25%), 118 in area 2 (59%), and 31 in area 3 (16%; Fig. 1). Fifty-six patients (28%) were converted to open parathyroidectomy. Mean operative time corresponded to 65±21 and 86±32 min in the 144 non-converted and 56 converted patients, respectively (p<0.0001).

The most common cause for conversion was lack of intraoperative localization (pathological gland not found) in 22 patients (11%). In all these 22 patients, enlarged gland was found after conversion where it was localized on preoperative ultrasound and sestamibi exams. These 22 abnormal glands were localized in area 1, 2, and 3 in four (18%), 12 (55%), and six (27%) patients, respectively. Difficult dissection (difficulty with dissection or a large adenoma taking up most of the working space) caused conversion in 20 patients (10%). Intraoperative bleeding was observed in seven patients (4%) during trocars positioning (anterior jugular vein in six patients and internal jugular vein in one patient). In those patients, bleeding was not controlled effectively though the 10-mm incision and led to conversion. Less frequent causes for conversion were due to inappropriate drop in IOPTH results in four patients (2%) and general causes in three patients (1%; Table 2). Intraoperative PTH results leading to conversion corresponded to a less than 50% decrease in two patients after initial node resection and in two patients with a double adenoma. General causes corresponded to intraoperative cardiovascular modifications that led to conversion in order to decrease operative time duration. Conversion rates and causes were similar between first 100 patients and last 100 patients (Table 2). No significant difference was observed between converted and non-converted patients versus preoperative biochemical parameters (unsuppressed PTH with a high normal or elevated calcium), CaPTHus score (≥3), ultrasound and sestamibi

Table 1 Patients characteristics

	All patients	First 100 patients	Last 100 patients	p Value
Preoperative calcium (mmol/L)	2.8±0.2	2.8±0.2	2.7±0.2	
Preoperative PTH (pg/mL)	173±274	184±376	163±112	
Strictly concordant Sestami/US	188 (89%)	89 (89%)	89 (89%)	
CaPTHus score<3/≥ 3	23/177	10/90	13/87	
Side right/left	92/108	46/54	46/54	
Operative time (min)	71±26	75±28	67±23	0.04
Localization area 1/2/3	51/118/31	24/63/13	27/55/18	

CaPTHus dichotomous scoring model to identify patients with single-gland disease [9]; *Localization area* resected gland locations were classified according to Henry classification [7]

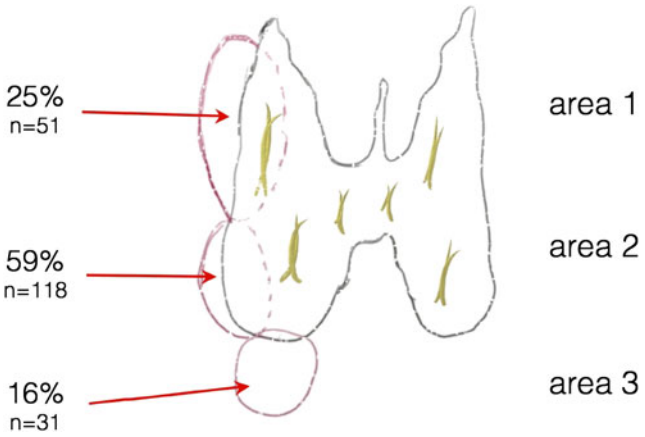

Fig. 1 Resected gland localization according to data from surgical exploration (Henry classification) [7]

findings (strictly concordance), and adenoma localization (area 3; Tables 2 and 3).

According to Clavien classification, postoperative morbidity was 6% (two patients were in class 1 (hyperthermia, malaise), eight patients in class 2 (pulmonary infection, urinary infection, wound inflammation, conjunctivitis), and one patient in class 3 (ICU for heart attack)). There was no mortality. Transient recurrent laryngeal nerve palsy was observed in five patients (2.5%) and remained permanent in one patient (0.5%). Eleven patients (5.5%) had a transient postoperative hypocalcemia. There were no cases of permanent hypoparathyroidism. Mean hospitalization duration was 3.3 days (from 2 to 8 days), and this duration was similar between converted and non-converted patients (3.4 versus 3.3).

Mean postoperative follow-up was 13±13 (6–72) months, and 196 patients (98%) were cured. One patient after appropriate drop in intraoperative PTH by >50% had a persistent disease. This patient on re-exploration underwent a subtotal parathyroidectomy for multiglandular disease (hyperplasia). Three patients developed recurrent disease at four (two patients) and five (one patient) years after endoscopic parathyroidectomy. At reoperation, two patients had a second adenoma (double adenoma), and one patient has not undergone reoperation. After surgical exploration, pathology results, and follow-up data, 194 (97%) and six patients (3%) were considered to have uniglandular and multiglandular disease, respectively. Interestingly, all six patients with multiglandular disease had a CaPTHus score of 3 or higher.

Table 2 Causes for conversion to cervicotomy

Causes for conversion	All patients	First 100 patients	Last 100 patients	*p* Value
Pathological gland not found	22 (11%)	9 (9%)	13 (13%)	
Localization area 1	4	1	3	
Localization area 2	12	7	5	
Localization area 3	6	1	5	
Difficult dissection	20 (10%)	9 (9%)	11 (11%)	
Localization area 1	7	2	5	
Localization area 2	10	5	5	
Localization area 3	3	2	1	
Bleeding	7 (4%)	5 (5%)	2 (2%)	
Localization area 1	2	2	0	
Localization area 2	4	2	2	
Localization area 3	1	1	0	
IOPTH negative results	4 (2%)	3 (3%)	1 (1%)	
Node resection	2	2	–	
Double adenoma	2	1	1	
General causes	3 (1%)	2 (2%)	1 (1%)	
Asystoly	1	1	–	
Hypercapnia	1	1	–	
Arrythmia	1	–	1	
All causes	56 (28%)	28 (28%)	28 (28%)	

IOPTH negative results intraoperative PTH did not fall by <50%; *Localization area* resected gland locations were classified according to Henry classification [7]

Table 3 Relations between conversion and patients characteristics

	Converted patients (n=56)	Non-converted patients (n=144)	*p* Value
Unsuppressed PTH	7 (12%)	9 (6%)	0.15
CaPTHus≥3	47 (84%)	130 (90%)	0.22
Strictly concordant ultrasound and sestamibi findings	47 (84%)	130 (90%)	0.22
Localization area 3	13 (23%)	18 (13%)	0.08

CaPTHus dichotomous scoring model to identify patients with single-gland disease [9]; *Localization area* resected gland locations were classified according to Henry classification [7]; *Unsuppressed PTH* unsuppressed preoperative PTH with a high normal or elevated calcium

Discussion

There is no consensus on what defines minimally invasive parathyroidectomy. However, most endocrine surgeons agree that an incision of 2.5 cm or less with minimal dissection (adenoma excision and no dissection of the normal glands) fulfills the criteria [3, 4, 11, 12]. In 2010, minimally invasive selective parathyroid surgery is well established and widely performed worldwide [1, 2]. However, literature review and international surveys have also shown that most common approaches for minimally invasive parathyroidectomy correspond in fact to open

mini-incision (about 70%), followed by video-assisted approach without gas insufflation (about 20%), and totally endoscopic lateral approach with gas insufflation (about 10%) [2, 5, 6, 13]. For totally endoscopic lateral approach (Henry technique), evaluation has been made by five retrospective studies from Marseille group and one comparative studies [4, 7, 8, 12, 14, 15]. This study is the first prospective study evaluating totally endoscopic lateral parathyroidectomy in a large number of patients. We showed that more than half of all patients with PHPT can undergo totally endoscopic lateral parathyroidectomy with a 98% cure rate. This approach was associated with complications rates similar to conventional techniques. However, conversion rate remained an important issue (28%) and patient selection, disease severity, and adenoma localization had no significant impact on conversion rate.

There is consensus that appropriate patient selection for single gland disease is the clue for a successful selective parathyroidectomy [2, 5]. These selected patients are considered to represent from 50% to 75% of all patients with PHPT depending of geographic area, type of patients referral, parathyroid imaging quality, type of selection (on imaging findings only or associated with biological data), and surgeon's experience [16, 17]. For totally endoscopic lateral parathyroidectomy, this percentage was 56% among 644 patients with PHPT in the largest series from Marseille group [14]. This study had similar results and confirmed that more than half of PHPT patients (52%) can undergo totally endoscopic lateral parathyroidectomy. Moreover, selective parathyroidectomy has been shown in randomized trials to have good success rates (>95%) [2, 5, 9]. This study confirmed that totally endoscopic lateral parathyroidectomy had a more than 97% cure rate in selected PHPT patients [7, 8, 12, 14, 15]. Similarly, we observed as previous series that postoperative permanent recurrent and parathyroid morbidity rates were low (0.5% and 0%, respectively) [4, 7, 8, 12, 14, 15].

An important finding in this study is that 28% of patients had to be converted to cervicotomy. Previous evaluations reported a conversion rate varying from 13% to 25% [4, 14, 15]. Hessman et al. described that 25% of the 68 patients that underwent totally endoscopic lateral parathyroidectomy were converted [4]. Interestingly, main causes were difficulties in adenoma localization, bleeding, and difficult dissection. At a lesser extent, Henry et al. reported that 13% among 365 patients were converted [14]. Four main causes were adenoma not found but correctly localized preoperatively, IOPTH negative results leading to multigland disease diagnosis, sestamibi false positive results, and difficult dissection. Our findings are in concordance with these previous series. Additionally, we showed that conversion rates and causes for conversion were similar in the first versus last 100 patients. This emphasizes that learning curve cannot be considered as a valid explanation for conversion rate and causes. Interestingly, lack of intraoperative adenoma localization (although correctly localized on preoperative exams) remained the main cause for conversion in previous series as in current study [4, 14]. This emphasizes that anatomic landmarks may be difficult to find when using totally endoscopic approach. Overall, these data support the fact that video-assisted techniques and more specifically totally endoscopic lateral approach are likely more difficult to master and perform than open minimally invasive parathyroidectomy [4]. This is a potential explanation of the low acceptance rate of this technique. We believe that a threshold of 30 patients per surgeon and per year might be a means to decrease conversion rate associated to this technique.

We also tried to define predictive factors for conversion. We observed that neither patients selection (CaPTHus score, strictly concordance of ultrasound and sestamibi), disease severity (unsuppressed PTH with high normal or elevated calcium), or adenoma localization (area 3) had a significant impact on conversion rate. Consequently, none of these criteria can be used as predictive factor for conversion to cervicotomy. This also emphasizes that totally endoscopic lateral parathyroidectomy has correct results in terms of conversion even when preoperative exams are not strictly concordant. In contrast to the Marseille group, we did not found that adenoma localized superficially and anteriorly at the level of or below the tip of the inferior pole of the thyroid lobe (area 3) had a significantly higher risk of conversion [7]. Consequently, we do not use a mini-open anterior approach for those patients and continue to use totally endoscopic lateral approach to resect pathologic gland localized in this area. In this study, IOPTH results leading to conversion were rare but helped to decrease the rate of persisting disease (two patients with double adenoma). Even if this study was not designed to evaluated IOPTH results, and cost-effectiveness analysis was not taken into account, these data support the use of intraoperative PTH monitoring in patients selected for totally endoscopic lateral parathyroidectomy [18, 19].

In this subset of patients selected for totally endoscopic lateral parathyroidectomy, patients with multiglandular disease are rare but remain an issue [14, 20]. Similarly to previous papers, this study showed that 3% of selected patients had multigland disease eventually [14]. Ultrasound and sestamibi scintigraphy are considered to predict with a high degree of certainty (90% and higher) whether an individual patient's PHPT is due to a single adenoma and represent the most frequently used way to select patients [2, 5, 17]. Because calcium and parathormone levels were significantly higher in single gland primary hyperparathyroidism, these two preoperative biological criteria have been used along with preoperative imaging findings to

improve patients' selection. Thus, CaPTHus score was proposed to identify patients with PHPT due to single-gland disease with a positive predictive value of 100% in patients with score of 3 or higher [9]. However, the study data do not support this conclusion since all six patients with multiglandular disease had a CaPTHus score of 3 or higher. We acknowledge several biases in this study. Recurrent laryngeal morbidity was not routinely evaluated but in patients with voice discomfort only. This may underestimate actual recurrent laryngeal morbidity rate. All patients in this study had a routine postoperative follow-up of 1 year. After that period, patients were followed up by their general practitioner and referred to us only if a recurrence was observed. We acknowledge that this strategy may underestimate actual postoperative cure rate because some patients could have recurred and not been sent back for reoperation (or reoperated elsewhere).

In conclusion, this study provides prospective evaluation of totally endoscopic lateral parathyroidectomy technique showing good postoperative results but high rate of conversion to cervicotomy. However, as stated almost 10 years ago, we continue to believe that among other minimally invasive approaches, this totally endoscopic technique has the major advantage in offering a good and magnified peroperative view that allows precise, careful dissection with minimal risks [15].

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