No Need to Abandon Focused Parathyroidectomy: A Multicenter Study of Long-term Outcome After Surgery for Primary Hyperparathyroidism

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Objective: The aim of this study was to investigate long-term outcomes after focused parathyroidectomy (FPTX) and open 4-gland parathyroid exploration (OPTX) for primary hyperparathyroidism (pHPT).

Background: Concerns about increased long-term recurrence rates after FPTX in conjunction with decreased operative times for OPTX have led some groups to abandon FPTX in favor of routine 4-gland exploration.

Methods: This is a multicenter retrospective cohort study of patients undergoing parathyroidectomy for pHPT from 1990 to 2013. The patient cohort was divided into 2 groups, FPTX and OPTX, based on intention-to-treat analysis. The primary outcome measure was the persistence of pHPT. Secondary outcome measures were differences in the long-term recurrence rate of persisting pHPT and surgical complications.

Results: A total of 4569 patients (3585 females) were included. The overall persistence and recurrence rates were 2.2% and 0.9%, respectively, after a median follow-up of 6.5 years. There were 2531 FPTX cases and 2038 OPTX cases. The initial persistence rate was higher for FPTX than for OPTX (2.7% vs 1.7%, $P = 0.036$); however, the long-term recurrence rate was not different (5-year 0.6% vs 0.4%, log-rank $P = 0.08$). Complications were more common in OPTX than in FPTX (7.6% vs 3.6%, $P < 0.001$).

Conclusions: FPTX was associated with fewer operative complications and an equivalent rate of long-term recurrence than with OPTX. Although initial persistence rates were higher after FPTX than after OPTX, most were readily resolved with subsequent early reoperation. FPTX should not be abandoned in patients with positive preoperative localization.

Keywords: bilateral exploration, focused, hyperparathyroidism, long-term outcome, parathyroidectomy

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Primary hyperparathyroidism (pHPT) is a common endocrine disorder characterized by hypersecretion of parathyroid hormone (PTH) from 1 or more parathyroid glands.[1] The resultant effect of hypercalcemia leads to significant morbidity and mortality if left untreated, including osteoporosis, renal stones, fatigue, and depression.[2,3]

The only definitive treatment is surgery, with the first successful parathyroidectomy for hyperparathyroidism being performed in Vienna in 1925.[3–5] From this date until the early 1990s, parathyroidectomy traditionally involved open bilateral exploration of all 4 parathyroid glands (OPTX) with excision of the enlarged gland(s). However, most cases of pHPT are caused by a single adenoma, and there has been a growing trend toward image-guided focused parathyroidectomy (FPTX), which involves preoperative localization, followed by a focused or unilateral exploration through a limited incision.[2,3,6–9] The feasibility of FPTX relies on accurate preoperative localization of a single parathyroid adenoma with sestamibi and/or ultrasound imaging.[10,11] FPTX offers improved cosmesis through a smaller incision and decreased complications such as pain, operation time, and duration of stay while increasing cost-effectiveness and quality of life.[6,12–16] It may be executed with or without intraoperative parathyroid hormone (IOPTH) measurements. Proponents for IOPTH measurement during FPTX claim decreased persistence rates, whereas opponents are concerned about unnecessary exploration due to false-negative IOPTH drops, increased operative time and an increased risk of surgical complications, and decreased cost-efficiency.[6,7,17–23]

Despite the benefits of FPTX, recent studies have questioned its durability with lower long-term cure rates than bilateral exploration. A recent retrospective study of 15,000 parathyroidectomies showed a significant increase in recurrence after FPTX compared with OPTX. IOPTH measurements were never used and approximately 5% of FPTX cases and only 0.4% of OPTX cases recurred by 10 years' time ($P < 0.001$).[24] This drive to abandon FPTX is further aided by a prospective study that showed that despite concordant preoperative localization scans (sestamibi and ultrasound) and a more than 50% IOPTH drop, up to 16% of multigland disease was missed using gross appearance at OPTX as a standard of reference.[25] Other studies have shown a statistically significant increase in the rate of long-term recurrence in FPTX compared with OPTX (2.5% vs 2.1%)[26,27] or a higher cure rate after FPTX than after OPTX.[15,18,20,26–28] All these latter studies used IOPTH as an adjunct to define extent of resection.

To date, there is an ongoing quest for the surgical approach with the lowest recurrence and complication rates, with many endocrine surgeons maintaining that there is no need to abandon unilateral parathyroidectomy,[29] as advocated by others.[24] The aim of this study was to examine the persistence, recurrence, and complication rates in a cohort of 4500 parathyroidectomies performed across the 2 largest Australian Endocrine Surgical Units without the adjunct of IOPTH.

METHODS

Patients and Study Design

This is a multicenter retrospective cohort study of all patients undergoing parathyroidectomy for pHPT at the University of Sydney Endocrine Surgical Unit and the Monash University Endocrine Surgery Unit from 1990 to 2013 (Monash 1993–2013). pHPT was defined by a high calcium level and a nonsuppressed PTH level, or a normal-high calcium level and a high PTH level with no of evidence of secondary hyperparathyroidism. Patients with secondary hyperparathyroidism, lithium-associated HPT, family history of

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pHPT, multiple endocrine neoplasia, familial hypocalciuric hypercalcemia, hyperparathyroidism-jaw tumor syndrome, parathyroid cancer, previous parathyroidectomy at other center, or only thoracic surgery were excluded (Fig. 1). All available baseline data such as sex, age, preoperative calcium levels, preoperative PTH levels, number of glands resected, weight of the resected glands, and concomitant thyroid surgery were recorded. As there were several different analyses and thus reference values for PTH during the study period, these levels were recalculated with the upper limit of the used reference values to fit our most recent reference value (15–68 ng/L). The patient cohort was divided into 2 groups, based on operative approach.

Group 1 comprised patients who were subjected to FPTX based on positive concordant functional and anatomic imaging, that is, a strongly positive sestamibi scan in combination with ultrasound scan or, alternatively, an unequivocally positive 4-dimensional computed tomographic scan. Generally, the focused approach utilized was a mini-incision procedure involving a 2- to 3-cm keyhole incision either laterally at the medial edge of the sternocleidomastoid muscle or centrally, depending on surgeon's preference. The aim of the operation was to identify and remove a parathyroid adenoma concordant with the imaging, and the ipsilateral gland was not routinely examined. Failure to locate an adenoma, or incidental finding of 2 enlarged ipsilateral glands, would prompt conversion to bilateral 4-gland exploration. Neither the γ-probe nor intraoperative ultrasound scan was used in this study. PTH levels were measured 1 to 2 hours and day 1 postsurgery to confirm cure (drop in the normal reference level) before informed discharge. However, within the context of this study, only patients with persisting high calcium levels were considered persistent cases. IOPTH measurements were not used routinely to confirm cure or guide the extent of dissection.

Group 2 comprised patients who underwent OPTX, mainly due to nonlocalizing or equivocal imaging or concomitant thyroid pathology requiring surgery. The bilateral operation aimed to visualize all 4 parathyroid glands, and in cases where no adenoma was found at normal anatomical sites, exploration of extended normal and ectopic sites was performed.

Routine workup and follow-up consisted of preoperative and postoperative laryngoscopy, 2-week clinical follow-up, and serum calcium levels at 3 to 12 months. If serum calcium level was normal at 3 to 12 months, further follow-up was undertaken by the patient's physician and such routine follow-up was received by the units. All data, including cases of persisting and recurrent disease, were entered into prospective surgical databases maintained within the University of Sydney Endocrine Surgical Unit and the Monash University Endocrine Surgery Unit. Treatment failure was divided into persistent or recurrent disease, based on documentation of hypercalcemia in combination with an inappropriately suppressed PTH within 6 months or more of surgery, respectively. Hypercalcemia was defined as a calcium level above the upper limit of corrected calcium in our laboratory values (2.55 mmol/L = 10.2 mg/dL). A small number of patients had a delayed 3-month postoperative calcium value taken between 6 and 12 months postsurgery, and these were therefore, if elevated, also noted as persistence (n = 3). PTH was not routinely followed up in normocalcemic patients postoperatively, with the exception of patients initially undergoing surgery for normocalcemic hyperparathyroidism, where a PTH value above normal reference value was considered persistence/recurrence.

Both groups were principally defined by intention to treat (ITT), which meant that the conversions were included in the ITT-FPTX group and not in the ITT-OPTX group. The primary outcome in this study was difference in the proportion of persistence rates between the ITT-FPTX and ITT-OPTX groups. However, the persistence rate was also analyzed on a "treatment received" (TR) basis, where all the conversions were included in the TR-OPTX group and not in the TR-FPTX group. Furthermore, a temporal comparison persistence rates to investigate any difference before and after the broad

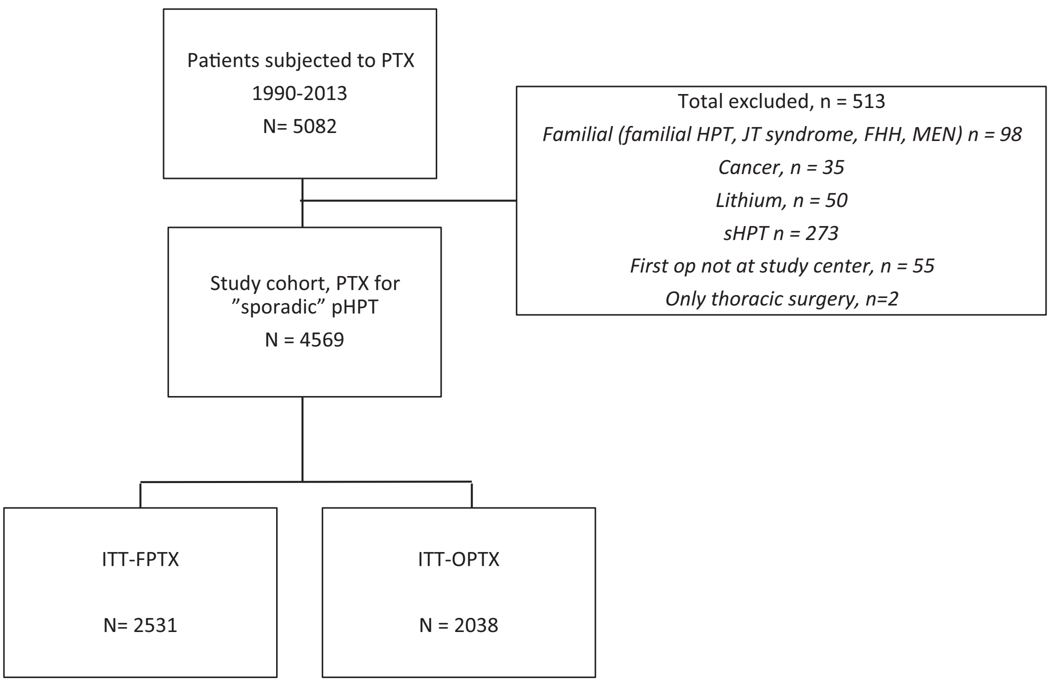

FIGURE 1. Consort diagram of enrolled patients. FHH indicates familial hypocalciuric hypercalcemia; JT, jaw tumor; MEN, multiple endocrine neoplasia; op, operation; PTX, parathyroidectomy; sHPT, secondary hyperparathyroidism. ITT-FPTX including conversions (n = 164).

introduction of FPTX at the study centers was performed. Other secondary outcomes measures studied were differences between the 2 groups regarding cumulative recurrence rates and proportion of complications. Specific complications noted were 30-day mortality, hypoparathyroidism, recurrent laryngeal nerve (RLN) palsy, wound infection, and hemorrhage. Hypoparathyroidism was defined as symptomatic hypocalcemia in need of additional calcium or vitamin D supplementation. Both RLN palsy and hypoparathyroidism were considered permanent if there was no recovery within 6 months. Hemorrhage was defined as a hematoma that required return to the operation theatre for clot evacuation.

Statistics

Statistics were performed with the SPSS software (version 20.0). The primary outcome, difference in the proportion of persistence rates after ITT-FPTX versus ITT-OPTX, was assessed with a χ^2 test and the sample size calculation with α of 0.05, power of 80%, needed 1533 persons in each group to show a difference between persistence rates of 1.5% and 3%. We included all patients available in our databases from year 1990 to maximize power. A Kaplan-Meier analysis and a log-rank test were performed to investigate any differences in long-term recurrence rates between groups. For the Kaplan-Meier analysis, ignore death censoring was used and all patients with persisting disease were excluded. Differences in baseline characteristics, complications, and persistence rates were assessed with the Student *t* test, Mann-Whitney *U* test, Fischer exact test, or χ^2 test, as appropriate.

Ethics

The study was approved by the relevant Human Research Ethics Committees.

RESULTS

A total of 5082 patients underwent parathyroidectomy during the study period, although 513 were excluded because of noted criteria (Fig. 1). A total of 4569 patients (3585 females) were included in the study cohort. Sixty-five percent of the patients (n = 2972) described at least 1 symptom or sign associated with hyperparathyroidism, and the remaining 35% (n = 1597) were asymptomatic and lacked signs of osteopenia at the time of surgery. After asymptomatic patients, who were generally treated because of young age, the most common primary indications for surgery were osteoporosis (n = 1474), neuromuscular disorders (n = 488), renal stones (n = 345), and neuropsychiatric disorders including fatigue (n = 372).

The median (range) follow-up was 6.5 (1.0–24.0) years. Serum calcium levels were available for more than 99% of patients within the first 12 months postsurgery. Of the 4569 patients, 103 cases persisted and 40 recurred during follow-up. To investigate outcome based on operative approach, 2 groups were formed on the basis of ITT analysis and they comprised 2531 ITT-FPTX cases, including 164 conversions, and 2038 ITT-OPTX cases. Baseline characteristics and operative data showed that the patient age was similar between the 2 groups, that the mean calcium and PTH levels were higher, and that there were fewer glands removed in the ITT-FPTX group. Furthermore, the proportion of patients undergoing concomitant thyroid surgery was smaller and the median weight of the resected glands was higher in the ITT-FPTX group (Table 1). The most common pathology indicating concomitant thyroid surgery was benign thyroid nodular disease (83%), followed by thyroid cancer (9%). FPTX became increasingly utilized from 1998 and is at present by far the most common procedure of the two (Fig. 2). To perform a temporal comparison to investigate any difference in persistence rates before and after the broad introduction of FPTX at the study centers, the cohort was divided on the basis of operation date. This analysis showed that for patients operated on before (n = 453) and after January 1, 1998 (n = 4116), the persistence rate was not statistically different at 1.3% and 2.4%, respectively ($P = 0.217$).

However, the primary outcome analysis showed that the persistence rate was higher in the ITT-FPTX group than in the ITT-OPTX group (2.7% vs 1.7%, $P = 0.036$). Furthermore, when the persistence rate was scrutinized by a TR instead of ITT analysis, the persistence rate was still higher for the patients who underwent TR-FPTX than for the patients subjected to TR-OPTX (2.7% vs 1.8%, $P = 0.043$; Table 2).

Overall, the long-term recurrence rates (excluding patients with persistence) were not statistically different between the ITT-FPTX and ITT-OPTX groups (log-rank $P = 0.080$; Fig. 3). Moreover, 5-year recurrence rates were very similar between the ITT-FPTX

TABLE 1. Patient Characteristics and Operative Details

Characteristics	ITT-FPTX*	ITT-OPTX	*P*
Female	1938 (76.6)	1647 (80.8)	<0.001
Age, mean (SD), yr	61.8 (13.9)	62.3 (14.1)	0.333†
Preop PTH, median (IQR), ng/L	123 (90–180)	107 (84–143)	<0.001‡
Preop calcium, median (IQR), mmol/L	2.77 (2.67–2.90)	2.69 (2.59–2.84)	<0.001‡
Postop calcium, median (IQR), mmol/L	2.35 (2.28–2.42)	2.31 (2.24–2.41)	<0.001‡
No. glands resected			
0	7 (0.3)	5 (0.3)	<0.001
1	2355 (93.0)	1501 (73.7)	
2	141 (5.6)	378 (18.5)	
3	13 (0.5)	70 (3.4)	
3,5	12 (0.5)	72 (3.5)	
4	3 (0.1)	11 (0.5)	
Weight of glands resected, median (IQR),§ mg	515 (270–1050)	383 (196–876)	<0.001‡
Concomitant thyroid surgery	381 (15.1)	1118 (54.9)	<0.001
Total	2531 (100)	2038 (100)	

Values within parentheses are percentages, unless otherwise indicated. *P* values are calculated with the χ^2 test unless otherwise indicated.
*ITT-FPTX including 164 conversions.
†Student *t* test.
‡Mann-Whitney *U* test.
§Total weight of all glands resected.
IQR indicates interquartile range; preop, preoperative; postop, 3-month postoperative calcium excluding persistent cases.

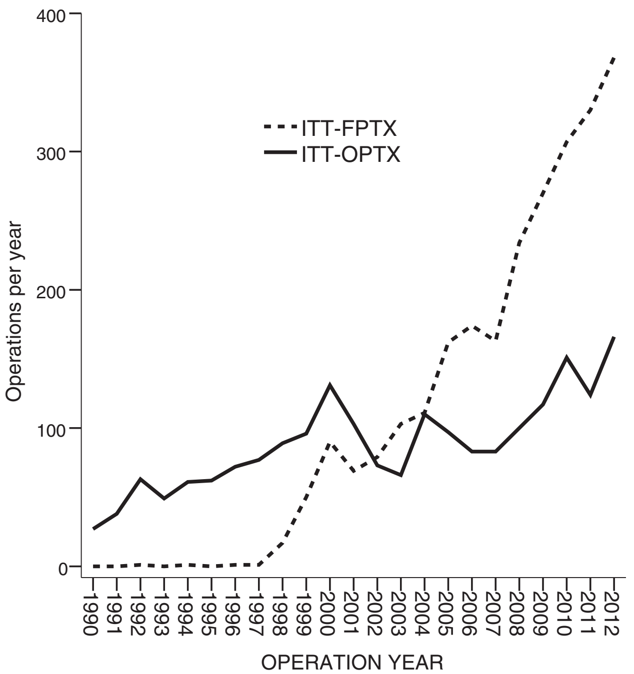

FIGURE 2. Number of operations performed each calendar year. Patients were included from January 1, 1990, to December 31, 2012. ITT-FPTX including conversions (n = 164).

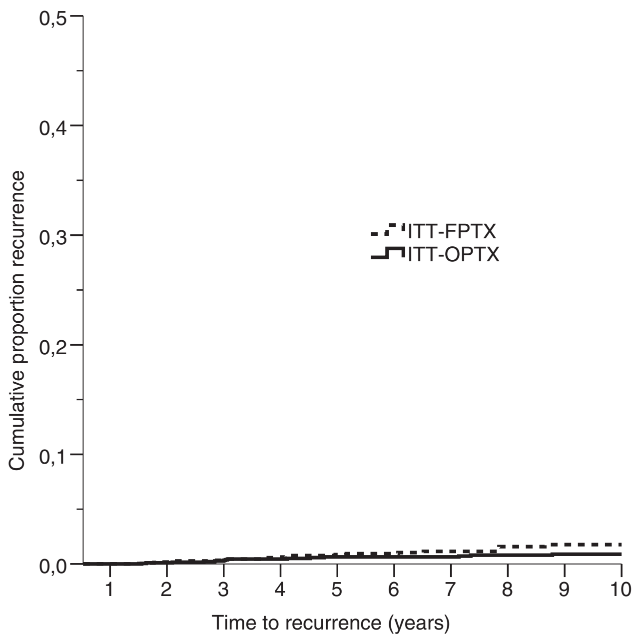

FIGURE 3. Long-term recurrence rates after FPTX and OPTX. Patients with persistent disease are excluded. ITT-FPTX including conversions (n = 164). Log-rank test for difference between groups showed $P = 0.080$.

TABLE 2. Persistence Rates After FPTX Versus OPTX by ITT and TR Analyses

Outcome	ITT-FPTX*	ITT-OPTX	P
Persistence	68 (2.7)	35 (1.7)	0.036
Total patients	2531 (100)	2038 (100)	
	TR-FPTX†	**TR-OPTX‡**	
Persistence	64 (2.7)	39 (1.8)	0.043
Total patients	2367 (100)	2202 (100)	

Values within parentheses are percentages. *P* values are calculated with the χ^2 test.
*ITT-FPTX including 164 conversions.
†TR-FPTX excluding the conversions.
‡TR-OPTX including 164 conversions.

TABLE 3. Complications After Parathyroidectomy

Complication	ITT-FPTX*	ITT-OPTX	P
30-d mortality	1 (0.1)	2 (0.2)	0.216†
RLN palsy temp	26 (1.2)	7 (0.8)	0.361
RLN palsy perm	7 (0.3)	4 (0.4)	0.893†
Hypoparathyroidism temp	17 (0.8)	27 (2.9)	<0.001
Hypoparathyroidism perm	2 (0.1)	2 (0.2)	0.588†
Hemorrhage	8 (0.4)	14 (1.5)	0.001
Wound infection	4 (0.2)	7 (0.8)	0.021†
Other	13 (0.6)	7 (0.8)	0.804
Sum of complications	78 (3.6)	70 (7.6)	<0.001
Total patients	2150 (100)	920 (100)	

Patients who had concomitant thyroid surgery (n = 1598) are excluded. Values within parentheses are percentages unless otherwise indicated. *P* values are calculated with the χ^2 test unless otherwise indicated.
*ITT-FPTX including conversions.
†Fischer exact test.
perm indicates permanent; temp, temporary.

and ITT-OPTX groups (0.6% vs 0.4%), but there was a trend toward a higher 10-year recurrence rate in the ITT-FPTX group than in the ITT-OPTX group (1.8% vs 0.9%; Fig. 3).

The long-term outcome of parathyroid surgery was further explored in the 3070 patients who were not subjected to concomitant thyroid surgery. There were 920 ITT-OPTX cases and 2050 ITT-FPTX cases in these subgroups, and the persistence rate was 2.2% and 2.3%, respectively ($P = 0.895$). The 5-year recurrence rate was 0.7% for the ITT-OPTX group and 0.8% for the ITT-FPTX group (log-rank $P = 0.144$). Thus, within this subgroup analysis, there was no difference in either persistence or long-term recurrence rates between groups. Complications after parathyroid surgery were analyzed after excluding the patients who underwent concomitant thyroid surgery to avoid bias between the ITT-FPTX and ITT-OPTX groups (Table 3). There were three 30-day mortalities in the cohort, but none of them were associated with the surgery or complications of surgery. The proportion of RLN injuries was not different between groups (Table 3), although 1 patient (0.1%) in the ITT-OPTX group suffered temporary bilateral palsy requiring prolonged intubation and temporary tracheostomy. Temporary hypoparathyroidism, despite routine postoperative calcium supplementation, was more common in the ITT-OPTX group (Table 3). The rate of wound infections and the sum of complications were also higher in the ITT-OPTX group than in the ITT-FPTX group (Table 3).

Subsequent Course for Patients With Persistence

The final pathology of the total 118 reoperative cases revealed hyperplasia defined as 3 or more diseased glands (n = 22), single adenoma missed at first operation (n = 22), ipsilateral double adenoma (n = 19), contralateral double adenoma (n = 38), mediastinal double adenoma (n = 2), and double adenoma with missing data of laterality (n = 3).

Ninety-three percent of the 68 patients (n = 63) with persistence in the ITT-FPTX group underwent reoperative surgery within 1 year (Table 4). Reoperations after OPTX were in general based on preoperative localization, although blind reoperation after FPTX did occur in some instances. At least one of the glands causing persistence was located on the contralateral side to the first operation in 33 cases (52%). Of the 63 ITT-FPTX patients with persistence, 21 patients had reoperative FPTX, 41 patients had reoperative OPTX, and 1 patient had surgery for a mediastinal gland with the result that all but 5 patients were cured. Hence, the number of patients with persisting pHPT at 1 year post–ITT-FPTX, including the result of reoperation was 10 (0.4%; Table 4). Nineteen patients in the ITT-OPTX group underwent reoperation within a year, and all of them were cured (Table 3). The number of patients with failure after 1 year accounting for reoperations in the ITT-OPTX group was thus 16 (0.8%; Table 4).

DISCUSSION

Over the last decade, FPTX guided by preoperative imaging has become the procedure of choice within the University of Sydney Endocrine Surgical Unit and the Monash University Endocrine Surgery Unit (Fig. 2). However, this is not an isolated Australian experience but rather a worldwide phenomenon.[9,15] In contrast, one of the largest centers, and previous proponents for FPTX, has recently reversed its position and now calls for an abandonment of FPTX.[24] Although others have responded to this in several publications confirming adequate results after FPTX with the use of IOPTH, this study examines the outcome after parathyroidectomy in a cohort of more than 4500 patients without the use of IOPTH.[3,6,15,17,26–28,30,31]

This study revealed an increase of 1 percentage point (2.7% vs 1.7%) for the immediate persistence rate, still the long-term recurrence rates were not significantly increased after FPTX as compared with OPTX. The 5-year recurrence rates were close to being identical between FPTX and OPTX (0.6% vs 0.4%; Fig. 3). Thus, to achieve an equivalent 5-year cure rate in patients undergoing FPTX and OPTX, 1 successful reoperation needs to be performed for every hundredth patient in the FPTX group. Because our units have had a strong local referral base, a 1 in a 100 return to surgery is not a big issue, although other groups go to great lengths to create a durable cure at initial surgery because most of their patients live far away.[24]

A subgroup analysis of the patients not subjected to concomitant thyroid surgery in this cohort showed no difference in persistence or long-term recurrence rates between the OPTX and FPTX groups, mainly due to a decreased persistence rate in the FPTX group. This increased cure rate after FPTX may be explained by exclusion of patients with multinodular goiter, as accuracy of preoperative imaging is decreased in such patients.

TABLE 4. Subsequent Course After Persistence

Outcome	ITT-FPTX*	ITT-OPTX	*P*
Persistence after first op	68 (2.7)	35 (1.7)	0.036
Reoperation within 1 yr	63 (2.5)	19 (0.9)	<0.001
Successful reoperation within 1 yr	58 (2.3)	19 (0.9)	<0.001
Failures† at 1 yr postop	10 (0.4)	16 (0.8)	0.012
Total patients	2531 (100)	2038 (100)	

Values within parentheses are percentages. *P* values are calculated with the χ^2 test.
*ITT-FPTX including conversions (n = 4).
†Patients who still had pHPT at 1 year postoperatively, including the result of reoperation, if any.

As mentioned, operative failures after both FPTX and OPTX occur mainly within 6 months, demonstrated by persistence rates for both surgical modalities greater than their respective recurrence rates. Fortunately, the subsequent course of these patients reveals a successful reoperation for most patients within 1 year. Although most of these reoperations were OPTX, approximately one third were cured with a second FPTX (Table 4). In 52% of reoperations in the FPTX group, at least one of the pathological parathyroid glands was located on the contralateral side and these patients would thus have needed OPTX to be cured.

Others report a 4% to 6% failure rate after FPTX at 10 years, which mirrors the experience in our study that unveils a combined 10-year cumulative persistence/recurrence rate of 4.5%.[24] However, the former study showed a 0.4% recurrence rate after OPTX whereas our study revealed a 2.7% combined 10-year cumulative persistence/recurrence rate.[24] As the previous study performed a majority of its OPTX cases in the most recent years, and the number of patients with 10- year follow-up is not quoted, inadequate follow-up may account for some difference between studies. Diversity in the definition of operative failure may also influence results. Whereas we have strictly used a calcium level above 2.55 mmol/L (10.2 mg/dL), the Tampa group used 10.0 mg/dL and normal PTH levels as their definition of operative failure, and this makes exact comparisons of results between cohorts difficult.[24]

Another study that supports the abandonment of FPTX showed that even a combination of preoperative imaging and IOPTH may fail to identify additional 16% of morphologically abnormal glands, thus suggesting that FPTX along with its operative adjuncts often misses multigland disease.[25] However, cohorts that have included the use of IOPTH exhibit 5-year recurrence rates after FPTX of 0.6% to 6.6%, and the clinical reality thus seems to be in marked contrast to that discovery.[15,18,24,26–28,31] Persistence rates after IOPTH-mediated FPTX may be slightly lower than FPTX without IOPTH; nevertheless, this approach has several drawbacks. Up to 9% of patients will be subjected to unnecessary conversion to bilateral exploration and operative time increases, and some patients will persist anyway.[23]

Although no statistically significant difference in long-term recurrence rates was shown between FPTX and OPTX, the cumulative recurrences rate in the FPTX group gradually increased more over time than in the OPTX group (Fig. 3). This raises some uncertainty as to whether the difference in recurrence rates will remain unchanged for 10 to 20 years' time, and this will only be elucidated as more patients reach this follow-up. Another theory that may have influenced the results of our study is that analysis done by ITT may actually artificially increase the rates of cure of FPTX, as conversions to OPTX are analyzed in the FPTX data.[26] Interestingly, this study actually points to the opposite, with higher persistence rates in the OPTX group after TR analysis. This may be explained by a selection bias of more patients with confirmed multiglandular disease included in the OPTX group.

Operative failure with recurrent hyperparathyroidism should be minimized, but the benefit of a more extensive dissection must be weighed against the risk of surgical complications. In concordance with previous literature, this study showed an increased risk of temporary hypoparathyroidism, hemorrhage, and wound infection in the OPTX group compared with the FPTX group.[14,15,32] Despite the fact that these are all potentially reversible complications, they can have devastating effects if not swiftly and prudently treated. Other significant but rare complications of bilateral exploration must also be considered. This is exemplified in this study wherein 1 patient suffered a temporary bilateral RLN palsy that resulted in a temporary tracheostomy after OPTX. Another benefit of focused operation may be shorter operative times, and although Norman et al[24] show similar operative times for bilateral and focused exploration, such results seem to be a consequence of a considerable learning curve and are not generalizable to most other centers.

Limitations of this study are mainly products of the retrospective nature of the data. As such, confounding by indication causing selection bias between groups is evident, as FPTX had higher preoperative calcium levels, higher PTH levels, and increased weight of parathyroid glands resected whereas OPTX was significantly associated with concomitant thyroid surgery. However, a time-dependent analysis was also performed, and although nonsignificant, a trend was noted toward a decreased persistence rate for patients treated before the introduction of FPTX (1.3% vs 2.4%), possibly reflecting a difference between surgical approaches. Also, as the data have been collected over a long period of time, the positive and negative predictive values of preoperative imaging may have changed. Unfortunately, only the future can tell whether long-term results after contemporary FPTX are different from historical FPTX due to any advance in accuracy of imaging modalities. Furthermore, follow-up data were collected in an assumption that recurrences will be notified and referral made to the original surgeon/institution and not to a different center. Although this assumption may be flawed and likely underestimates true biochemical recurrence rates to some extent, there is no reason to suspect bias between groups in this aspect. However, a possible bias would be that the treating physician following up a patient after parathyroidectomy may be more reluctant to refer a patient back to surgery after a previous OPTX than after a previous FPTX. The generalizability of our data to other centers that do use IOPTH during FPTX may be somewhat hampered by the fact that we have never used IOPTH measurements, although, theoretically, their long-term cure rate should be at least as good as ours compared with OPTX, with the tradeoff of occasional unnecessary conversion to bilateral exploration and increased operative time.[23]

CONCLUSIONS

Our experience confirms that FPTX guided by preoperative imaging remains a sound and successful approach for managing pHPT and that this procedure can be undertaken without concern of a significant increase in disease recurrence in the long term. The balance between operative complications and cure rates makes FPTX our favored approach in carefully selected patients with pHPT, as we believe that a 1% reoperative rate is a reasonable tradeoff when considering the decreased complication rate, decreased cost, and time saved by not performing OPTX on everyone.

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