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Reoperation for parathyroid adenoma: A contemporary experience

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Abstract

Background—We reviewed reoperations for persistent or recurrent sporadic parathyroid adenoma to evaluate and compare our current results and outcomes to our previous experience.

Methods—From 1996 to 2008, 237 patients with persistent or recurrent hyperparathyroidism after failed operation underwent reoperation. Patients were re-explored with the assistance of non-invasive and sometimes invasive imaging.

Results—A missed adenoma was suspected pre-operatively in 163 patients. Reoperation resulted in long-term resolution of hypercalcemia in 92%. Adenomas were in entopic locations in 32%; the most frequent ectopic location was the thymus (20%). Sestamibi scanning and ultrasonography were the most successful non-invasive imaging studies (96% positive predictive value (PPV) and 84% PPV respectively). Forty-four percent of patients had a reoperation based solely on non-invasive imaging. Of the invasive procedures performed, arteriography resulted in the best localization (92% PPV). Permanent recurrent laryngeal nerve injury occurred in 1.8%.

Conclusion—Compared to our prior experience (1982–1995), outcomes remained similar (92% resolution of hypercalcemia and 1.8% recurrent nerve injury currently versus 96% and 1.3% previously). Fewer patients received invasive studies for pre-operative localization (56% vs 73%, respectively). The decreased use of invasive imaging is due to technical improvements and greater confidence in the combination of ultrasonography and sestamibi scanning.

Contemporary success rates for initial cervical exploration for primary hyperparathyroidism (HPT) are reported to be greater than 96% for both directed and bilateral explorations,^{1–4} although this rate may be less when long-term follow-up is obtained.² Most common causes

of failure of initial exploration for primary HPT have been surgeon inexperience, ectopic location of parathyroid glands, and multigland disease.⁵

Success rates for re-exploration for persistent or recurrent primary HPT have been reported to be lower, ranging from 86% to 96%⁶⁻⁹ in series that included some patients with familial HPT and multigland disease. Other series have included only those patients presumed to have sporadic, missed adenoma as the etiology of HPT, and have reported success of 95% and better.^{10,11} Given the high risk of persistent or recurrent HPT in patients with multigland disease¹² as opposed to the very high likelihood of cure for patients with single adenoma at first operation, analyzing the latter group of patients separately allows for a focused assessment of localization and reoperative strategies. In this context, we analyzed our contemporary experience with reoperation for persistent or recurrent HPT for presumed adenoma.

METHODS

Between January 1996 and January 2008, 237 patients underwent operation at the National Institutes of Health (NIH) under a clinical protocol approved by our Institutional Review Board for recurrent or persistent primary HPT. During this time, approximately 10 cases were not referred for surgery due mainly to inadequate tumor localization, and 10 cases were treated by transarterial embolization in lieu of operative exploration. One hundred and sixty-three patients (69%) who were believed pre-operatively to have a single missed adenoma as the cause of their HPT underwent operative exploration (Fig 1).

The medical records of the 163 patients were reviewed retrospectively. Demographic information and signs and symptoms of HPT at evaluation were collected. Operative reports and pathology slides and reports from previous operations had been requested for each patient at the time of evaluation at the NIH; these reports were reviewed when available.

Based on our previously described systematic approach,¹¹ all 163 patients underwent non-invasive localization studies consisting of neck ultrasonography (US) with 10 or 7.5 mHz transducer, nuclear medicine scanning, computed tomography (CT), and magnetic resonance imaging (MRI). Nuclear medicine scanning was conducted using a standard protocol of injection of Tc-99 m-pertechnetate and Tc-99 m-sestamibi with early/delayed imaging, subtraction, oblique views, and single photon emission computed tomography (SPECT) as described previously.¹³ Patients with concordant information from two or more non-invasive studies and no discordant information underwent operative exploration; otherwise, patients underwent 1 or more invasive localization studies before operation.

Patients found to have potential but not definitive parathyroid lesions that were accessible to percutaneous aspiration on non-invasive localization underwent fine needle aspiration (FNA) guided by US or CT. If the aspirate did not result in a positive gradient of parathyroid hormone (PTH), or if there was no lesion based on noninvasive testing, patients underwent digital subtraction arteriography and selective trans-arterial hypocalcemic stimulation with nonselective venous sampling for PTH.¹⁴ For arterial stimulation venous sampling, a multi-sidehole pigtail type catheter was positioned in the upper superior vena cava (SVC) to obtain baseline blood samples, and additional timed (20 sec, 40 sec, and 60 sec) blood samples were obtained after each selective hypocalcemic (sodium citrate) arterial stimulation injection to test for release of PTH. A gradient was considered positive if the PTH level increased to 1.4 times or more above the baseline PTH value that was obtained from the SVC just prior to the corresponding arterial stimulation. If a clear blush was identified, the patient underwent operative exploration without further localization efforts.

Patients who still had no definitive localization after these studies underwent selective venous sampling (SVS) directed to the inferior, middle, and superior thyroid veins, as well as thymic and vertebral veins.¹⁵ Patients with a 2-fold gradient or more above the baseline value in the iliac vein were considered for exploration. In some cases, patients with a clear step-up on arterial stimulation venous sampling underwent SVS as well because we were still evaluating the utility of arterial stimulation sampling. The results of all localization studies and details of the operative procedures were collected. Intra-operative parathyroid hormone (IOPTH) assays were used routinely beginning in 1998; a decrease in the end-of-operation value of greater than 50% from baseline and removal of abnormal tissue was considered a positive IOPTH result. Data from IOPTH and intra-operative ultrasound (IOUS) were collected. Pathology reports and details of the hospital course were recorded for all patients. Follow-up data regarding symptoms, calcium values, and autograft status were collected when available.

Success at operation was defined as successful identification and extirpation of an adenoma; cure was considered long-term (>6 months) resolution of hypercalcemia. Pre-operative factors and utilization of localization studies were compared among patients in the current series; pre-operative data and outcomes were also compared to the previous series.¹¹ Binomial proportions were compared using the Fisher exact test. Ordered categorical parameters were compared between 2 groups using an exact Cochran-Armitage trend test.¹⁶ All *P* values are 2-tailed and presented without adjustment for multiple comparisons; however, in view of the number of tests performed, only *P* values < .01 were considered statistically significant, while those tests for which $.01 < P < .05$ were considered indicative of strong trends.

RESULTS

Features of HPT and previous operations

Demographic data for all patients are presented in Table I. Pre-operative serum calcium and PTH values are reported in Table I. Familial hypocalciuric hypercalcemia was excluded according to standard criteria.¹⁷ Asymptomatic patients were explored if the abnormal glands were well-localized on pre-operative imaging and the patients exhibited some symptom or sign(s) of primary HPT, even if these symptoms/signs were not able to be well categorized. Details of previous operations are presented in Table II.

Pre-operative tumor localization studies

Details of localization studies performed at the NIH prior to re-exploration are presented in Table III. Overall, sestamibi scanning had the greatest positive predictive value of the non-invasive localization studies (96%). One hundred and sixty-one patients underwent both sestamibi scanning and cervical US (Table IV). Of note, in the group of patients with discordant positive studies, 13 of the 14 false positive results were given by US. Nine of these adenomas were found at operation in the thymus and five in the neck. The 13 false positive US results indicated a lesion in the neck that did not prove to be the adenoma; 5 of these 13 studies identified a neck lesion that was not the site of the adenoma. Patients with mediastinal adenomas were analyzed separately. In these 40 patients, the PPVs for sestamibi scanning, CT, and MRI were 100%, 86%, and 77% respectively.

Seventy-one of the 163 patients (44%) underwent exploration without any invasive studies, while 92 (56%) patients went on to invasive imaging studies. US or CT-guided FNA gave the greatest PPV (100%), but only 15 patients had questionable parathyroid lesions amenable to the technique. Venous sampling by hypocalcemic arterial stimulation was performed with almost all arteriograms; this sampling yielded a similar PPV to the

arteriogram (Fig 2), although the localization was not as precise. Two patients were taken to the operating room with a positive result on hypocalcemic stimulation and negative arteriogram; the lesion was found in both. SVS was performed in only 37 patients. In the majority of these patients, there was some supporting information from other studies, but 14 patients were taken to the operating room based primarily on localization from SVS. The lesion was found in 11 of these patients (79%).

Operative procedures

One hundred and sixty-three patients underwent a total of 169 procedures (Table V). Six patients had both neck and mediastinal procedures during the same operation; these were considered as 2 procedures per patient. The locations of the 155 abnormal parathyroid adenomas found are shown in Fig 3. Adenomas were found in entopic locations in 53 patients (34%); the most frequent ectopic location was in the thymus (36 adenomas).

Intra-operative PTH (IOPTH) was used in 127 patients; the mean baseline and end-of-operation values are shown in Table V. The calculated sensitivity and specificity of IOPTH in this series were 99% and 80% respectively, with an accuracy of 98%. In 36 patients, IOPTH was not yet used and the assay was not performed; abnormal parathyroid tissue was found in all but one of these 36 patients. Intra-operative ultrasonography (IOUS) was used in 74 operations; in 58 of these 74 operations (77%), IOUS assisted the surgeon in localizing the adenoma while in 16 operations, IOUS was not useful. In 4 of these operations, the lesion was found in the thymus or another mediastinal site and was considered to be located too low to be found by IOUS. In another 3 patients, the exploration was negative. Therefore, in 9 instances, IOUS was used but did not assist in intra-operative localization of the adenoma.

Complications of these operations are also presented in Table V. Thirty-eight patients (23%) were discharged with calcium supplementation alone, and 49 patients were discharged with both calcium and a vitamin D analog (30%).

Outcome of operation

Short and long term results of reoperation for HPT at the NIH are shown in Table VI. Follow-up data beyond 6 months post-operation were obtained for 129 of the 163 patients (79%); 34 patients were lost to follow-up. Of these 34 patients, 16 patients were from outside the U.S., and attempts to contact them or their referring doctors were unsuccessful.

Abnormal parathyroid tissue was found or resolution of hypercalcemia occurred in 157 of 163 patients (96%); no abnormal tissue was found in 6 patients, all of whom remain persistently hypercalcemic. Two patients were found to have persistent hypercalcemia despite abnormal parathyroid tissue found at operation; these patients are presumed to have multigland disease that was not appreciated prior to reoperation. Two additional patients developed recurrent HPT in follow-up. Of interest, 70 of the 71 (99%) patients who underwent operation on the basis of non-invasive imaging alone were cured.

Statistical comparisons were made among pre-operative factors for the patients who had negative explorations ($n = 6$) and those who had successful explorations ($n = 157$). There was a strong trend toward more invasive procedures performed in the negative exploration group ($P = .019$).

Comparison to our previous results

Our current results were compared to our previous results.¹¹ Significant differences were found in the use of pre-operative localization. Patients underwent arteriography (66% vs

49% previous and current respectively) and selective venous sampling (43 vs 23%) more frequently in the previous series ($P < .01$ for both comparisons). The follow-up comparison (comparing the prior series fraction of 215/222 [97%] vs the current series fraction of 119/129 [92%] who were cured) has an associated Fisher exact test P value of .07. The comparison itself may be flawed because the interval of follow-up for the older group was less and therefore may overstate the fraction with long-term cure.

DISCUSSION

This large series of 163 patients undergoing reoperation in the contemporary era allows us to compare strategy and outcomes with previous experiences. We recommend a step-wise approach to pre-operative localization as follows.

Pre-operative localization: noninvasive modalities

Technetium-99m-sestamibi (MIBI) was first introduced for myocardial perfusion imaging in 1992 as an alternative to imaging with thallous chloride, and then evaluated in patients undergoing first operation for primary HPT; it was shown to be as effective as the thallous chloride combination for parathyroid localization with sensitivity of 90%.¹⁹ Double phase MIBI scintigraphy has been shown to be effective in the reoperative setting as well.^{13,20,21} SPECT images and oblique views further improved the sensitivity of scintigraphy to 92% for solitary adenomas in the reoperative setting.²¹

In a smaller previous series at our institution, the combination of high-resolution ultrasonography, using a 10 MHz transducer and double phase MIBI scanning was found to localize an adenoma correctly in 94% of previously operated cases.²² Analyses in the current series found similar results. In all cases where both US and MIBI were positive, including the 14 cases in which one result was a false positive, an adenoma was removed successfully. In the case where the US was positive and the MIBI was negative, an adenoma was removed successfully in 97% of cases and these were predominantly from the neck. In the case where the MIBI was positive and the US was negative, the success rate was less (91%) and just over half of the adenomas were found in the chest.

Given these findings, we recommend the following algorithm (Fig 4). We continue to recommend CT for patients who have an adenoma identified in the mediastinum by the MIBI; in these patients, CT had a greater PPV than MRI. We also recommend obtaining further cross-sectional imaging, usually a CT, to evaluate both the neck and the mediastinum in the case where the MIBI is positive and the US negative.

Pre-operative localization: invasive modalities

If localization is negative or equivocal on non-invasive imaging, invasive imaging is required. Based on our data, we recommend a stepwise approach to invasive procedures. The data in the current series for US or CT-guided FNA are similar to previous data from our institution²³ and continue to highlight the value of FNA in distinguishing parathyroid lesions from thyroid and other pathology. If a lesion is indeterminate but amenable to FNA, then FNA should be the first invasive procedure. If positive, FNA renders further invasive testing unnecessary.

Digital subtraction arteriogram should be the next invasive procedure attempted by an experienced arteriographer. Arterial stimulation venous sampling can be performed at the same time as the arteriogram and has a similarly high PPV. An equivocal localization by arteriogram may be confirmed with this sampling, eliminating the need to subject the patient to a selective venous sampling at another time. SVS is reserved for those patients who still do not have definitive tumor localization after arteriography and arterial stimulation venous

sampling. SVS should be performed after the arteriogram due to its improvement by venous anatomy information from arteriography,¹⁵ lesser utility, and less precise localization; often the procedure can only localize to a region or side of the neck.

Intra-operative maneuvers

IOUS and IOPTH were judged to be useful in this series in many instances; these data are similar to another recent report.⁶ The outcomes of this series, however, are not different from the outcomes of our previous series, in which IOPTH was not yet available.¹¹ These data and the distribution of adenomas found in both entopic and ectopic locations continue to highlight the need for the surgeon to be experienced in recognizing parathyroid adenomas by gross appearance and to be knowledgeable of parathyroid embryology and anatomy regardless of available operative tools. Frozen sections examined by an experienced pathologist should be used to differentiate parathyroid from other tissue.²⁴ A directed surgical approach is recommended, based on pre-operative localization.

In conclusion, the rates of success at operation and resolution of hypercalcemia are similar to our previous series¹¹ and compare favorably with other series.^{6–10} The most striking and important overall difference between the 2 series is the less frequent use of invasive imaging; 56% of patients in the current series versus 73% of patients in the previous series.¹¹ We attribute the difference to improved confidence in the non-invasive imaging and in particular to improvements in the methods of the nuclear medicine studies. Finally, follow-up beyond 6 months is recommended for a more complete understanding of recurrence patterns and rates of long-term hypocalcemia.

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References

1. van Heerden JA, Grant CS. Surgical treatment of primary hyperparathyroidism: an institutional perspective. *World J Surg.* 1991; 15:688–92. [PubMed: 1767534]
2. Bergenfelz A, Lindblom P, Tibblin S, Westerdahl J. Unilateral versus bilateral neck exploration for primary hyperparathyroidism. *Ann Surg.* 2002; 236:543–51. [PubMed: 12409657]
3. Allendorf J, DiGorgi M, Spanknebel K, Inabnet W, Chabot J, Legerfo P. 1112 consecutive bilateral neck explorations for primary hyperparathyroidism. *World J Surg.* 2007; 31:2075–80. [PubMed: 17768656]
4. McGill J, Sturgeon C, Kaplan SP, Chiu B, Kaplan EL, Angelos P. How does the operative strategy for primary hyperparathyroidism impact the findings and cure rate? A comparison of 800 parathyroidectomies. *J Am Coll Surg.* 2008; 207:246–9. [PubMed: 18656054]
5. Bruining HA, Birkenhäger JC, Ong GL, Lamberts SW. Causes of failure in operations for hyperparathyroidism. *Surgery.* 1987; 101:562–5. [PubMed: 3576448]
6. Richards ML, Thompson GB, Farley DR, Grant CS. Reoperative parathyroidectomy in 228 patients during the era of minimal-access surgery and intraoperative parathyroid hormone monitoring. *Am J Surg.* 2008; 196:937–43. [PubMed: 19095113]
7. Cheung PS, Borgstrom A, Thompson NW. Strategy in reoperative surgery for hyperparathyroidism. *Arch Surg.* 1989; 124:676–80. [PubMed: 2730318]
8. Brennan MF, Marx SJ, Doppman J, Costa J, Saxe A, Spiegel A, et al. Results of reoperation for persistent and recurrent hyperparathyroidism. *Ann Surg.* 1981; 194:671–6. [PubMed: 7305478]
9. Brennan MF, Norton JA. Reoperation for persistent and recurrent hyperparathyroidism. *Ann Surg.* 1985; 201:40–4. [PubMed: 2981520]
10. Shen W, Düren M, Morita E, Higgins C, Duh QY, Siperstein AE, et al. Reoperation for persistent or recurrent primary hyperparathyroidism. *Arch Surg.* 1996; 131:861–9. [PubMed: 8712911]

11. Jaskowiak N, Norton JA, Alexander HR, Doppman JL, Shawker T, Skarulis M, et al. A prospective trial evaluating a standard approach to reoperation for missed parathyroid adenoma. *Ann Surg.* 1996; 224:308–20. [PubMed: 8813259]
12. Saxe AW, Brennan MF. Reoperative parathyroid surgery for primary hyperparathyroidism caused by multi-gland disease: total parathyroidectomy and autotransplantation with cryopreserved tissue. *Surgery.* 1982; 91:616–21. [PubMed: 6123156]
13. Alexander HR, Chen CC, Shawker T, Choyke P, Chan TJ, Chang R, et al. Role of preoperative localization and intra-operative localization maneuvers including intraoperative PTH assay determination for patients with persistent or recurrent hyperparathyroidism. *J Bone Min Res.* 2002; 17(Suppl2):N133–40.
14. Miller DL, Chang R, Doppman JL, Norton JA. Localization of parathyroid adenomas: superselective DSA versus super-selective conventional angiography. *Radiology.* 1989; 170(3 Pt 2):1003–6. [PubMed: 2644666]
15. Sugg SL, Fraker DL, Alexander HR, Doppman JL, Miller DL, Chang R, et al. Prospective evaluation of selective venous sampling for parathyroid hormone concentration in patients undergoing reoperations for primary hyperparathyroidism. *Surgery.* 1993; 114:1004–10. [PubMed: 8256203]
16. Agresti, A. Categorical data analysis. New York: Wiley; 1990. p. 79-129.
17. Arnold, A.; Marx, SJ. Familial hyperparathyroidism (Including MEN, FHH, and HPT-JT). In: Rosen, C., editor. *Primer on the metabolic bone diseases and mineral metabolism.* 7. Washington, DC: American Society for Bone and Mineral Research; 2009.
18. Feldman AL, Sharaf RN, Skarulis MC, Bartlett DL, Libutti SK, Weinstein LS, et al. Results of heterotopic parathyroid autotransplantation: a 13-year experience. *Surgery.* 1999; 126:1042–8. [PubMed: 10598186]
19. Taillefer R, Boucher Y, Potvin C, Lambert R. Detection and localization of parathyroid adenomas in patients with hyperparathyroidism using a single radionuclide imaging procedure with technetium-99m-sestamibi (double-phase study). *J Nucl Med.* 1992; 33:1801–7. [PubMed: 1328564]
20. Chen CC, Skarulis MC, Fraker DL, Alexander HR, Marx SJ, Spiegel AM. Technetium-99m-sestamibi imaging before re-operation for primary hyperparathyroidism. *J Nucl Med.* 1995; 36:2186–91. [PubMed: 8523102]
21. Civelek AC, Ozalp E, Donovan P, Udelsman R. Prospective evaluation for delayed technetium-99m-sestamibi SPECT scintigraphy for preoperative localization of primary hyperparathyroidism. *Surgery.* 2002; 131:149–57. [PubMed: 11854692]
22. Feingold DL, Alexander HR, Chen CC, Libutti SK, Shawker TH, Simonds WF, et al. Ultrasound and sestamibi scan as the only preoperative imaging tests in reoperation for parathyroid adenoma. *Surgery.* 2000; 128:1103–10. [PubMed: 11114649]
23. MacFarlane MP, Fraker DL, Shawker TH, Norton JA, Doppman JL, Chang RA, et al. Use of preoperative fine-needle aspiration in patients undergoing reoperation for primary hyperparathyroidism. *Surgery.* 1994; 116:959–64. [PubMed: 7985103]
24. Livolsi VA, Hamilton R. Intraoperative assessment of parathyroid gland pathology. A common view from the surgeon and the pathologist. *Am J Clin Pathol.* 1994; 102:365–73. [PubMed: 8085562]

Fig 1. Distribution of patients according to diagnosis who underwent reoperation for persistent or recurrent hyperparathyroidism at the National Institutes of Health from January 1996 to January 2008.

Fig 2. Functional and anatomical localization studies for patient with persistent phpt due to adenoma in right tracheoesophageal (TE) groove. (A) Parathyroid arterial stimulation venous sampling. Samples obtained from catheter placed in the superior vena cava. A pronounced (5-fold) step-up in parathyroid hormone (PTH) is demonstrated after sodium citrate (hypocalcemic stimulation) injection of right thyrocervical arterial bed. (B) and (C) Hypervascular mass (*arrows*) consistent with right TE-groove parathyroid adenoma demonstrated on computed tomography (B) and digitally subtracted arteriogram (C).

Fig 3.

Location and frequency of 155 parathyroid adenomas found at reoperation. (1) Tracheoesophageal groove: 28 (18%); (2) anterior mediastinum/thymus: 36 (23%); (3) entopic upper position: 28 (18%); (4) entopic lower position: 25 (16%); (5) intra-thyroidal: 3 (2%); (6) undescended: 14 (10%); (7) carotid sheath: 13 (8%); (8) retroesophageal: 4 (3%); (9) other mediastinal location: 4 (3%)

Fig 4. Proposed approach to patients with persistent or recurrent primary hyperparathyroidism due to suspected missed adenoma.

Table IPatient characteristics (*n* = 163)

	n	%
Male	57	35
Female	106	65
Mean age at NIH operation (yrs) $\pm$ SEM	51.5 $\pm$ 1.1	
Range of age at NIH operation (yrs)	16–78	
History of neck radiation	13	8
Presentation		
Asymptomatic patients	27	17
Patients with 1 symptom or sign	136	83
Symptoms and signs		
Fatigue	75	46
Nephrolithiasis	74	45
Neuropsychiatric	51	31
Bone pain	31	19
Gastrointestinal complaints	28	17
Muscle weakness	14	9
Nocturnal polyuria	10	6
Fractures	6	3.7
Bone densitometry (at NIH; data available for 139 pts)		
Osteopenia (2.5 < worst T score < 2.0)	24	17
Osteoporosis (worst T score $\geq$ 2.5)	74	53
Neither	41	30
Mean T score $\pm$ SEM	−2.6 $\pm$ 0.1	
Range of T score	−6.3–2.7	

Biochemical evaluation assay	NIH normal range *	Mean pre-operative ($\pm$ SEM)	Mean discharge ($\pm$ SEM)	Mean -%Δ ($\pm$ SEM)
Venous ionized calcium (mmol/L)	1.22–1.38	1.54 (0.01)	1.23 (0.01)	19.9 (0.7)
Intact parathyroid hormone (pg/mL)	16–87	151.9 (12.1)	23.7 (2.1)	77.4 (2.4)

* Current NIH normal range; normal ranges have varied slightly during the time period of this study.

Table II

Details of previous operations and procedures

	Operation		
	First	Second	Third
Number of operations	163 [*]	41	5
Procedure			
Neck exploration	157	34	3
Four glands	146	19	1
Directed	11	15	2
Mediastinal approach	1	2	3
Median sternotomy	1	1	1
Thoracoscopy	0	1	0
Details not recorded	0	0	2
Unknown	6	5	0
Parathyroid biopsied/resected			
No parathyroid tissue removed	28	24	5
One gland	52	7	0
Two glands	38	8	0
Three glands	25	0	0
Four glands	8	0	0
Unknown	12	2	0
Result			
Persistent	150	41	5
Recurrent	13	0	0
Mean time to recurrence (yrs) ($\pm$ SEM)	6.2 (1.4)		
Range of time to recurrence (yrs)	1–16		
Additional procedures			
Thyroid procedure	49	18	2
Lobectomy or portion of lobe	39	17	2
Total or subtotal	10	1	0
Transcervical thymectomy	31	7	1
Immediate autograft	2	0	0
Removal of autograft	0	0	0
Mediastinal lesion ablation attempt	8		

^{*} One patient had both a neck and mediastinal exploration at first operation.

Table IIIPre-operative localization studies at NIH ($n = 163$)

	n	%		
Patients who underwent operation with non-invasive studies only	71	44		
Patients who underwent operation with at least one non-invasive study	92	56		

Localization study (%)	Number performed (%)	True positive (%)	False positive (%)	PPV
Non-invasive				
Neck ultrasound (US)	161 (99)	97 (60)	19 (11)	84
Sestamibi	163 (100)	113 (69)	5 (3)	96
CT, neck/chest	162 (99)	78 (48)	21 (13)	79
MRI, neck/chest	157 (96)	66 (42)	17 (11)	80
Invasive				
US or CT guided FNA	15 (9)	12 (80)	0 (0)	100
Arteriogram	80 (49)	49 (61)	4 (5)	92
Arterial stimulation venous sampling	72 (44)	34 (47)	3 (4)	92
Selective venous sampling	37 (23)	27 (73)	5 (14)	84

PPV, Positive predictive value; FNA, fine needle aspirate.

Table IV

Ultrasound and sestamibi analyzed together ($n = 161$)

US Result	Sestamibi result	<i>n</i>	Location of adenoma		Success at operation (%)
			Neck	Chest	
+	+	69 (concordant)	63	6	69 (100)
+	+	14 (discordant)	5	9	14 (100)
+	-	32	26	5	31 (97)
-	+	34	15	16	31 (91)

Table V

NIH operations in 163 patients

	n	
Total operations	163	
Total procedures	169	
Neck procedures	151	
Exploration		
Unilateral	140	
Bilateral	11	
Incision		
Transcervical	119	
Along sternocleidomastoid muscle	32	
Mediastinal procedures	18	
Median sternotomy	11	
Thoracotomy	4	
Thoracoscopy *	2	
Mediastinoscopy *	1	
Additional procedures		
Thyroid lobectomy	9	
Subtotal or total thyroidectomy	0	
Thymectomy	44	
Transcervical	32	
Mediastinal approach	12	
Immediate autograft	9	
Removal of autograft	0	
Intra-operative intact PTH		
Number of patients tested	127	
Mean baseline ($\pm$ SEM)	213 (26)	
Mean last value ($\pm$ SEM)	24.4 (2.7)	
Mean $-\% \Delta$ ($\pm$ SEM)	83.9 (1.4)	
Complication (N = 163)	n	%
Recurrent laryngeal nerve injury		
Temporary	6	3.7
Permanent	3	1.8
Pneumonia	2	1
Wound infection	1	0.6
Peri-operative deaths	0	0
Severe hypocalcemia		
Requiring Vitamin D analog	47	29
Requiring intravenous calcium	6	3.7
Requiring subsequent autografts	6	3.7

* One thoracoscopy and 1 mediastinoscopy each were converted to thoracotomy for technical reasons.

Table VI

Results of operation

	n	%
Operative success in 163 patients [*]	157	96
Long-term results		
>6 months follow-up data available	129/163	79
Lost to follow-up	34/163	21
Mean length of follow-up (yrs) ($\pm$ SEM)	6.55 (0.3)	
Range (yrs)	0.5–12.76	
Calcium status in follow-up ($n = 129$)		
Hypercalcemic	10	8
Persistent	8	
Recurrent (TTR 6 and 12 yrs)	2	
Normocalcemic	105	81
Hypocalcemic [†]	14	11
Autograft follow-up		
Number placed	17/163	10
At time of NIH operation for HPT	9	
In follow-up	8 [‡]	
Result (follow-up available for 14 grafts) ¹⁸		
Hyperfunctioning	0	
Functioning	3/14	21
Partially functioning	3/14	21
Failed	8/14	57

^{*} Abnormal parathyroid tissue found and/or resolution of hypercalcemia).

[†] Considered hypocalcemic if autograft was required in follow-up.

[‡] Two patients had 2 autografts placed.