Minimally Invasive Radio-guided Surgery for Hyperparathyroidism: An Experience with Tc-99m Sestamibi

Ali Jangjoo (MD)[1], Mohammad Naser Forghani (MD)[2], Mostafa Mehrabibahar (MD)[1], Vahid Reza Dabbagh Kakhki (MD)[3], Seyed Rasoul Zakavi (MD)[3], Kamran Aryana (MD)[3], Abbas Abdollahi (MD)[2], Ramin Sadeghi (MD)[3]

[1]General Surgery Department, Imam Reza Hospital, [2]General Surgery Department, Omid Hospital, [3]Nuclear Medicine Research Center, Imam Reza Hospital, Mashhad University of Medical Sciences Mashhad, Iran

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ABSTRACT

Introduction: Radio-guided parathyroid surgery along with other minimally invasive surgeries constitutes the main surgical treatment procedures for different kinds of hyperparathyroidism. In this article we have reported our experience of radio-guided parathyroid surgery using Tc-99m sestamibi.
Methods: Ten patients with hyperparathyroidism included in our study. Twenty mCi of Tc-99m sestamibi was injected intravenously to the patients in the day of surgery. All patients underwent surgery 4 hours after injection of the tracer. Abnormal parathyroid glands were localized by surgical gamma probe during surgery and were removed.
Results: Eight out of 10 patients had single adenoma. One patient had parathyroid hyperplasia secondary to chronic renal failure. The one remaining patient had persistent hyperparathyroidism with previous unsuccessful parathyroid surgeries. Except for the patient with parathyroid hyperplasia, parathyroid hormone (PTH) level of all other patients decreased after surgery including the patient with persistent hyperparathyroidism.
Conclusion: Minimally invasive radio-guided parathyroid surgery is an easy and safe method for surgical treatment of hyperparathyroidism. With the increasing availability of surgical gamma probes and nuclear medicine facilities in Iran considering this kind of approach for surgical treatment of hyperparathyroidism seems rational.

Key words: Minimally invasive radio-guided surgery, Hyperparathyroidism, Tc-99m sestamibi, Parathyroid adenoma, Parathyroid hyperplasia

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Corresponding author: Ramin Sadeghi, Assistant Professor, Nuclear Medicine Research Center, Imam Reza Hospital, Mashhad University of Medical Sciences, Ebn Sina Street. Mashhad, Iran.
E-mail: sadeghir@mums.ac.ir

INTRODUCTION

Hyperparathyroidism is a common disease which can go undetected for a long period. Primary hyperparathyroidism is the main type of this disorder which is usually due to a solitary adenoma. Multiple adenomas, hyperplasia, and parathyroid carcinoma are the other causes (1,2). Secondary hyperparathyroidism is usually the result of renal failure (3,4). Failure to localize the pathologic glands during surgery is a serious problem which can be largely avoided by pre-surgical localization. For this purpose nuclear medicine procedures play an important role using Tc-99m sestamibi and/or Thalium-201 scanning (5-8).

Bilateral cervical neck dissection for removal of all hyper-functioning parathyroid tissues was considered the treatment of choice in different types of hyperparathyroidism (9). However for solitary parathyroid adenoma removal of the diseased gland is curative approach. With introduction of pre-operative localization by nuclear medicine imaging, unilateral approach became more and more popular (10). Gradually minimally invasive parathyroid surgery with endoscopy or video assistance was introduced and with the advent of gamma probes, radio-guided surgery has become a favorable procedure for parathyroid adenoma (9, 11-15). This approach is also gaining popularity for secondary and tertiary hyperparathyroidism, (16-18), parathyroid cancer (19) as well as difficult cases such as ectopic adenoma or post-surgical persistent hyperparathyroidism (20-25). To the extent of our knowledge, this approach has not been reported previously in Iran.

In this study we presented our experience in minimally invasive radio-guided parathyroid surgery using Tc-99m sestamibi.

METHODS

Ten patients with hyperparathyroidism entered in our study. We didn't recruit any patient with concomitant thyroid nodule. The day of study all patients received 20 mCi of Tc-99m sestamibi intravenously. Five minutes as well as three hours post-injection anterior projection images (5 min per view) of the neck and mediastinum were taken using low-energy high resolution collimator, Tc-99m photopeak and 20% window (Figure 1).

Four hours after radiotracer injection, patients underwent general anesthesia for surgical removal of abnormal parathyroid tissues. All quadrants of the neck were explored using a gamma probe (Europrobe, GMS, France). After spotting the hottest point, a 3 cm incision was made over the point. Plathysma and strap muscles were retracted and under the guide of gamma probe the hot parathyroid tissues were removed. The sternocleidomastoid muscle and jugular vein were also identified. Especial care was taken to preserve the recurrent laryngeal nerve.

Background counts of the neck over the carotid arteries as well as ex-vivo counts of the removed parathyroid tissues were also recorded.

Pre and post-operative PTH levels were recorded. We didn't use any intra-operative approach (such as intra-operative PTH measurement, or frozen section) for confirmation of abnormal parathyroid tissue removal.

RESULTS

Ten patients entered in our study. Summary of the patients' data are available in Table 1. Nine patients were female and the mean age of the patients was 43.8 years. The etiology of hyperparathyroidism was single adenoma in 8 patients. Patient number 4 had parathyroid hyperplasia secondary to chronic renal failure. Patient number 9 had previous unsuccessful surgeries for single parathyroid adenoma resection and underwent surgery due to persistent hyperparathyroidism. In all patients abnormal parathyroid glands were localized in pre-operative Tc-99m sestamibi scan.

Figure 1. Delayed anterior image of a patient with a parathyroid adenoma in the right upper part of the thyroid.

Table 1. Summary of patients' data.

No	Age	Gender	Tc-99m sestamibi scan results	Etiology	Location of abnormal parathyroid tissue	Ex vivo parathyroid to carotid artery count	Size of the excised gland (cm)	Time to completion of surgery (min)	Outcome of surgery
1	49	F	Positive	Adenoma	Left lower	1.4	2	27	Cure
2	42	F	Positive	Adenoma	Left lower	1.3	3	27	Cure
3	46	F	Positive	Adenoma	Left lower	0.5	2	37	Cure
4	40	F	Positive in lower poles of thyroid	Hyperplasia due to CRF	Two excised nodes in the left lower and right lower	0.25/0.25	2/1.5	45	Persistent disease
5	41	F	Positive	Adenoma	Left lower	0.8	2	30	Cure
6	44	F	Positive	Adenoma	Right lower	0.9	1.5	30	Cure
7	51	F	Positive	Adenoma	Right upper	1.1	3	30	Cure
8	50	F	Positive	Adenoma	Left upper	1	2	24	Cure
9	35	M	Positive	Persistent hyerparathyroidism due to failed excised adenoma	Right lower	1.1	3	25	Cure
10	40	F	Positive	Adenoma	Left lower	0.9	2	30	Cure
Mean	43.8					0.863	2.18	30.5	

In all patients with parathyroid adenoma (including patient number 9 with persistent hyperparathyroidism) the abnormal gland was successfully located during surgery by gamma probe and excised, and successfully as proven by PTH measurement. In patient number 4 with parathyroid hyperplasia; despite removal of two abnormal glands, hyperparathyroidism persisted after surgery.
Six out of 11 excised parathyroid glands were located in the lower part of the left thyroid lobe. Three in right lower, one in right upper and one was in left upper part of the thyroid lobe. The mean size of the excised glands was 2.18 cm.

DISCUSSION

In recent years, the worldwide trend in parathyroid surgery is toward less invasive procedures: from bilateral neck exploration to unilateral neck exploration and more recently several types of minimally invasive interventions including radio-guided surgery (26). The most important advance in the management of hyperparathyroidism which allowed these minimally invasive procedures was pre-operative localization of the abnormal parathyroid glands. Parathyroid imaging is usually performed with Tc-99m sestamibi which is avidly accumulated in the parathyroid adenomas. Two techniques of subtraction or dual phase scintigraphy both were successful (5-7). At our department, we use dual phase technique with 20 mCi Tc-99m sestamibi. The overall sensitivity of Tc-99m sestamibi scanning for pre-operative localization of abnormal parathyroid glands is reported to be 77%. The false negative results are more likely to happen in patients with small or superior adenomas, hyperplasia or preoperative normocalcemia (27). Although it is recommended not to perform radio-guided surgery in patients with negative Tc-99m sestamibi scan, Lal et al. reported localization of abnormal parathyroid glands in 18% of these patients. However it seems prudent to perform other localization procedures such as Thalium-201 or ultrasonography in this context (28).
Another breakthrough in the management of hyperparathyroidism was intra-operative PTH assay (14, 29). In our department, we didn't have access to this assay. However except for the patient with hyperplasia, surgery was successful in the remaining of the cases. Our results are in agreement with Caudle et al and Goldstein et al which had excellent results without intra-operative PTH assay (30, 31).
Although the radiation dose to the surgical staff during radio-guided parathyroidectomy is low (8.78 to 11 µSv for senior surgeon in the study of Bekiş et al (32)), Rubello et al developed a low dose radio-guided surgery with excellent results (33, 34). However this needs significant skill (35) and we chose the conventional high dose Tc-99m sestamibi injection for surgery. In addition to parathyroid adenoma, secondary and tertiary hyperparathyroidism due to parathyroid hyperplasia could also be considered for radio-guided surgery. In the largest study in this field Chen et al. reported excellent result in secondary/tertiary hyperparathyroidism patients (36). In our study, surgery in the only patient with secondary hyperparathyroidism was not successful. Further patients with secondary hyperparathyroidism should be recruited in order to be able to reach any conclusion concerning these groups of patients.
Difficult cases of hyperparathyroidism including ectopic, persistent and recurrent parathyroid adenomas were also treated with radio-guided surgery (22-24). Our patient with persistent hyperparathyroidism had several failed previous surgeries and his recurrent laryngeal nerve was severed. It was a difficult case which was cured with radio-guided surgery. The count ratio of the abnormal parathyroid glands to the background (carotid artery area in our study) is reported to be more than 20% in the study of Murphy et al. (37). We also used this rule in our patient. The mean target to

background ratio was 0.863 in our patients. The lowest ratio was for the patient with parathyroid hyperplasia which is in agreement with Rubello et al. who found lower target to background ratio in hyperplastic lesions (34).

The main advantages of minimally invasive radio-guided parathyroid surgery are reported to be small incisions with better cosmetic results, increased accuracy for detection of abnormal parathyroid tissues especially in ectopic adenomas and other difficult cases (38), and significant cost saving due to reduced surgery time (39). In our study, the mean time of the surgery was also significantly short (30.5 min) which can decrease the morbidity and cost of surgery.

CONCLUSION

Minimally invasive radio-guided parathyroid surgery is readily available and valuable tool for treatment of the hyperparathyroidism. This approach can be very helpful in difficult cases such as ectopic adenomas or persistent hyperparathyroidism. With increasing availability of surgical gamma probes and nuclear medicine facilities in Iran, considering this kind of surgery for hyperparathyroid patients seems a rational approach. Lack of other kinds of minimally invasive parathyroid surgery in Iran (such as video assisted surgery) underscores the importance of radio-guided procedures.

REFERENCES

1. Hedayat A, Kachueian N. A survey of 110 cases of primary hyperparathyroidism in Dr.Shariati Hospital and the results of localizing the adenoma via MIBI scanning. Tehran Univ Med J 1998; 56(4): 35-39 [Persian].
2. Mir Saeed Ghazi AA, Bostani I, Nasri H, Amiri Z, Rahimi F, Nafarabadi T et al. Primary hyperparathyroidism: A report on 30 cases of the disease. J Shahid Beheshti Univ Med Sci Health Serv 2000; 21(4): 301-308 [Persian].
3. Ranjbar Omrani GH, Dabbagh Manesh MH, Soleimani M, Roozbeh J, Raiss Jalali GA, Behzadi S. Predictive factors for persistent hyperparathyroidism after kidney transplantation. Arch Iran Med 2005; 8(4): 295-299.
4. Rahimian M, Sami R, Behzad F. Prevalence of secondary hyper parathyroidism in hemodialysis patients. J Shahid Sadoughi Univ Med Sci Health Serv 2007; 1: 1-8 [Persian].
5. Eftekhari M. Thallium-Technetium subtraction parathyroid imaging in evaluation of surgically implanted parathyroid tissue. Iran J Nucl Med 1993; 1:50-53 [Persian].
6. Greyson ND. Imaging of parathyroid lesions with radionuclides. Is it worth done? Iran J Nucl Med 1995;3:1-10.
7. Zakavi SR, Saghari M. Sensitivity and specificity of Thallium-Technetium subtraction scan in localization of the parathyroid adenoma. Iran J Nucl Med 1995; 3: 2-7 [Persian].
8. Fard Esfahani A, Aryana K, Eftekhari M, Vakili A, Saghari M. Localization of ectopic parathyroid adenoma with Tc-99m-MIBI. Iran J Nucl Med 1998; 8-9: 11-17 [Persian].
9. Bergenfelz A, Kanngiesser V, Zielke A, Nies C, Rothmund M. Conventional bilateral cervical exploration versus open minimally invasive parathyroidectomy under local anaesthesia for primary hyperparathyroidism. Br J Surg 2005; 92(2):190-197.
10. Bergenfelz A, Lindblom P, Tibblin S, Westerdahl J. Unilateral versus bilateral neck exploration for primary hyperparathyroidism: a prospective randomized controlled trial. Ann Surg 2002; 236(5): 543-551.
11. Giraldez-Rodriguez LA, Giraldez-Casasnovas LJ. Minimally invasive parathyroidectomy as treatment for primary hyperparathyroidism. Bol Asoc Med P R 2008; 100(1): 27-32.
12. Untch BR, Barfield ME, Bason J, Olson JA Jr. Minimally invasive radio-guided surgery for primary hyperparathyroidism. Ann Surg Oncol. 2007; 14(12): 3401-3402.
13. Somashekhar SP, Gupta P, Ballal S, Parameshwaran, Zaveri SS, Venkatachala et al. Minimally invasive radioguided surgery for parathyroid adenomas (MIRP). Natl Med J India 2007; 20(1): 13-15.
14. Rubello D, Mariani G, Pelizzo MR. Minimally invasive radio-guided parathyroidectomy on a group of 452 primary hyperparathyroid patients: refinement of preoperative imaging and intraoperative procedure. Nuklearmedizin 2007; 46(3): 85-92.
15. Davies M, Fraser WD, Hosking DJ. The management of primary hyperparathyroidism. Clin Endocrinol 2002; 57(2): 145-155.
16. Jorna FH, Jager PL, Lemstra C, Wiggers T, Stegeman CA, Plukker JT. Utility of an intraoperative gamma probe in the surgical management of secondary or tertiary

hyperparathyroidism. Am J Surg 2008; 196(1): 13-18.
17. Ogi S, Fukumitsu N, Uchiyama M, Mori Y, Takeyama H. The usefulness of radio-guided surgery in secondary hyperparathyroidism. Ann Nucl Med 2004; 18(1):69-71.
18. Navarra G, Feggi L, Ascanelli S, Turini A, Carcoforo P, De Paoli E et al. Role of radio-guided surgery in recurrent secondary hyperparathyroidism. Nephron 2001; 88(1): 36-38.
19. Placzkowski K, Christian R, Chen H. Radioguided parathyroidectomy for recurrent parathyroid cancer. Clin Nucl Med 2007; 32(5): 358-360.
20. Moncet D, Isaac G, Staltari D, Tomasello A, Boronat S. Ectopic mediastinal parathyroid adenoma. Detection with a radioisotopic probe and resolution with videothoracoscopy. Medicina (B Aires) 2006; 66(5):457-460 [Spanish].
21. Quagliata A, Lopez JJ, Juri C, Alonso O. Value of radioguided surgery with dobutamine 99mTc-MIBI in persistent secondary hyperparathyroidism. Rev Esp Med Nucl 2006; 25(6): 387-390 [Spanish].
22. Cayo A, Chen H. Radioguided reoperative parathyroidectomy for persistent primary hyperparathyroidism. Clin Nucl Med 2008; 33(10): 668-670.
23. Uludag M, Isgor A, Yetkin G, Atay M, Kebudi A, Akgun I. Supernumerary ectopic parathyroid glands. Persistent hyperparathyroidism due to mediastinal parathyroid adenoma localized by preoperative single photon emission computed tomography and intraoperative gamma probe application. Hormones (Athens) 2009; 8(2): 144-149.
24. Ott MC, Malthaner RA, Reid R. Intraoperative radioguided thoracoscopic removal of ectopic parathyroid adenoma. Ann Thorac Surg 2001; 72(5): 1758-1760.
25. Rubello D, Piotto A, Pagetta C, Pelizzo M, Casara D. Ectopic parathyroid adenomas located at the carotid bifurcation: the role of preoperative Tc-99m MIBI scintigraphy and the intraoperative gamma probe procedure in surgical treatment planning. Clin Nucl Med 2001; 26(9): 774-776.
26. Phitayakorn R, McHenry C. Parathyroidectomy: Overview of the anatomic basis and surgical strategies for parathyroid operations. Clinic Rev Bone Miner Metab 2007; 5(2): 89-102.
27. Merlino JI, Ko K, Minotti A, McHenry CR. The false negative technetium-99m-sestamibi scan in patients with primary hyperparathyroidism: correlation with clinical factors and operative findings. Am Surg 2003; 69(3): 225-229.
28. Lal A, Chen H. The negative sestamibi scan: is a minimally invasive parathyroidectomy still possible? Ann Surg Oncol 2007; 14(8): 2363-2366.
29. Chen H, Mack E, Starling JR. A comprehensive evaluation of perioperative adjuncts during minimally invasive parathyroidectomy: which is most reliable? Ann Surg 2005; 242(3): 375-380.
30. Caudle AS, Brier SE, Calvo BF, Kim HJ, Meyers MO, Ollila DW. Experienced radio-guided surgery teams can successfully perform minimally invasive radio-guided parathyroidectomy without intraoperative parathyroid hormone assays. Am Surg 2006; 72(9): 785-789.
31. Goldstein RE, Billheimer D, Martin WH, Richards K. Sestamibi scanning and minimally invasive radioguided parathyroidectomy without intraoperative parathyroid hormone measurement. Ann Surg 2003; 237(5): 722-730.
32. Bekis R, Celik P, Uysal B, Kocdor MA, Atila K, Saydam S et al. Exposure of surgical staff in surgical probe applications in radioguided parathyroidectomy. Eur Arch Otorhinolaryngol 2008; 265(12):1545-1548.
33. Rubello D, Fig LM, Casara D, Piotto A, Boni G, Pelizzo MR et al. Radioguided surgery of parathyroid adenomas and recurrent thyroid cancer using the "low sestamibi dose" protocol. Cancer Biother Radiopharm 2006; 21(3): 194-205.
34. Rubello D, Piotto A, Medi F, Gross MD, Shapiro B, Erba P et al. 'Low dose' 99mTc-Sestamibi for radioguided surgery of primary hyperparathyroidism. Eur J Surg Oncol 2005; 31(2): 191-196.
35. Inabnet WB, Kim CK, Haber RS, Lopchinsky RA. Radioguidance is not necessary during parathyroidectomy. Arch Surg 2002; 137: 967-970.
36. Chen H, Mack E, Starling JR. Radioguided parathyroidectomy is equally effective for both adenomatous and hyperplastic glands. Ann Surg 2003; 238(3): 332-337.
37. Murphy C, Norman J. The 20% rule: a simple, instantaneous radioactivity measurement defines cure and allows elimination of frozen sections and hormone assays during parathyroidectomy. Surgery 1999; 126(6): 1023-1028.
38. Rubello D, Giannini S, Martini C, Piotto A, Rampin L, Fanti S et al. Minimally invasive radio-guided parathyroidectomy. Biomed Pharmacother 2006; 60(3): 134-138.
39. Flynn MB, Bumpous JM, Schill K, McMasters KM. Minimally invasive radioguided parathyroidectomy. J Am Coll Surg 2000; 191: 24-31.