

## Focused, Minimally Invasive Radio-Guided Parathyroidectomy: A Feasible and Safe Option for Elderly Patients with Primary Hyperparathyroidism

Menahem Ben Haim MD<sup>1</sup>, S.T. Zwas MD<sup>2</sup>, Yaron Munz MD<sup>1</sup>, Dan Rosin MD<sup>1</sup>, Esther L. Shabtai MSc<sup>3</sup>, Joseph Kuriansky MD<sup>1</sup>, David Olchovsky MD<sup>4</sup>, Oded Zmora MD<sup>1</sup>, Alexander Scarlat MD<sup>5</sup>, Amram Ayalon MD<sup>1</sup> and Moshe Shabtai MD<sup>1</sup>

Departments of <sup>1</sup>Surgery and Transplantation, Endocrine Surgery Service, <sup>2</sup>Nuclear Medicine and <sup>4</sup>Internal Medicine A, and <sup>5</sup>Division of Anesthesiology and Intensive Care, Sheba Medical Center, Tel Hashomer, Israel

<sup>3</sup>Statistical Service, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel

Affiliated to Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel

**Key words:** minimally invasive, parathyroidectomy, parathyroid scintigraphy

### Abstract

**Background:** Primary hyperparathyroidism in elderly patients is usually associated with additional co-morbidity that increases operative risk, and thus many geriatric patients are denied the benefit of surgery for a single parathyroid adenoma.

**Objectives:** To evaluate the safety and efficacy of accurate single photon emission computed tomography sestamibi scintigraphy, enabling precise localization of a single adenoma, in the geriatric population

**Methods:** Twenty-two patients aged 70 years and over with biochemically proven PHPT and with a single parathyroid adenoma identified by localization studies (sestamibi SPECT scan and ultrasonography) underwent 23 operations over 29 months (out of a total of 140 patients operated upon during the same period). Immediate preoperative sestamibi scintigraphy and marking of focal adenoma uptake followed by intraoperative hand-held gamma probe were used for the removal of the parathyroid adenoma by unilateral minimal access surgery. Associated major co-morbid conditions and pre- and postoperative calcium, phosphorus and parathormone levels were recorded. Indications for surgery were listed and operative and postoperative complications were noted. The patients were followed for a mean period of 17.7 months using the same parameters.

**Results:** The 22 patients with PHPT had a mean age of 76.3 ± 5.9 years (range 70–88 years) and a female to male ratio of 13:9. Associated co-morbidity included ischemic heart disease (n=15), hypertension (n=22), non-insulin-dependent diabetes mellitus (n=9), chronic obstructive pulmonary disease (n=3), and previous neck surgery (n=3). Mean preoperative serum calcium, phosphorous and PTH were 11.7 ± 1.3 mg/dl, 2.5 ± 0.5 mg/dl and 160.9 ± 75.4 pg/ml respectively. In 20 of the 22 patients, surgery was successful in curing PHPT (91%). One patient had persistent hypercalcemia due to a missed adenoma, and repeat operation (by focused minimal access surgery) was successfully performed 2 weeks later. There were no complications and no morbidity postoperatively. Mean postoperative serum calcium, phosphorous and PTH were 9.6 ± 1.2 mg/dl, 3.0 ± 0.5 mg/dl and 35.2 ± 24 pg/ml respectively. In all patients, serum calcium levels remained normal (9.7 ± 1.3 mg/ml) after long-term follow-up (mean 17.7 ± 9.6 months).

**Conclusions:** Minimally invasive, radio-guided focused parathyroidectomy for a single adenoma is a safe and effective method to cure hyperparathyroidism in the elderly. Success of surgery is directly related to the surgeon's experience and to the precise localization marking provided by sestamibi scintigraphic SPECT localization and concurrent sonographic findings.

*IMAJ 2003;5:326–328*

Since primary hyperparathyroidism in the elderly patient is often associated with co-morbid conditions that increase operative risk, these patients may be denied the benefit of surgical treatment [1]. The advent of accurate localizing methods for a single parathyroid adenoma [2–4], together with continued, accumulating evidence that unilateral focused removal of a single adenoma can achieve the same cure rates (95%) as formal bilateral neck exploration [5–7], has changed the approach to the surgical treatment of parathyroid adenoma in the elderly population [8,9]. The increasing proportion of elderly individuals in western society, combined with an incidence of >1.5% of HPT in this patient population [9] and the significant morbidity caused by this condition, constitute a considerable incentive to evaluate the role of focused, minimal access parathyroidectomy in the geriatric population. The present study analyzes the data from 22 patients older than 70 years of age who underwent surgery for a single adenoma diagnosed biochemically and localized preoperatively by technetium-99m sestamibi SPECT scan and/or sonography, from a single center over a 29 month period. The application of this method to elderly patients, the indications for surgery, postoperative complications, immediate as well as longer period follow-up results are discussed, and the success of minimally invasive surgery in alleviating PHPT in the elderly is evaluated.

### Patients and Methods

Twenty-two patients aged 70 and over, out of 140 patients, underwent 23 focused, minimally invasive parathyroidectomies for a single parathyroid adenoma over a 29 month period. In all patients the diagnosis was based on the finding of high serum levels of calcium and PTH. The preoperative localization studies in all patients included technetium-99m sestamibi planar (early and delayed) SPECT scan combined with a Tc-99m thyroid scan and cervical ultrasonography.

PHPT = primary hyperparathyroidism

SPECT = single photon emission computed tomography

PTH = parathormone

Demographic data, associated morbidity, indication for surgery, pre- and postoperative serum calcium, phosphorus and PTH levels, size of adenoma, operation time, postoperative morbidity and mortality, and long-term serum calcium levels were entered into a database and analyzed. Success and failure to identify the adenoma were correlated with the agreement between preoperative localization studies and the experience of the surgeon.

### Localization studies

Scintigraphic localization was performed using dual isotope (Tc-99m sestamibi for parathyroids and Tc-99m-pertechnetate for thyroid) SPECT scintigraphy according to the following protocol: intravenous injection of 15 mCi of Tc-99m-MIBI with sequential planar neck and mediastinum views for 30 minutes followed by a SPECT view of the same region for 30 minutes. Delayed planar scans followed until a full visualization of a hot-spot concentration was noted with its complete wash-out within 90–120 minutes. A thyroid scan with 2 mCi of Tc-99m-pertechnetate followed 10 minutes after i.v. injection of the tracer to outline thyroid gland uptake. In addition, all patients underwent a high resolution ultrasonographic scan of the neck. The site of the adenoma indicated by each modality was recorded and compared to the actual site found at surgery. All patients had an additional planar Tc-99m-MIBI scan 2–4 hours prior to surgery, and the site on the skin overlying the known adenoma hot spot was marked on the patient's skin using a radioactive point-source marking indicated by a small ink cross.

### Surgery

All patients were operated on under general anesthesia using an endotracheal tube. A small horizontal incision of 1.5–2 cm was made over the skin marking, and the deep cervical space was entered by splitting the strap muscles. A hand-held gamma probe (Europrobe®, France) was used to locate the adenoma, if not identified immediately, and to obtain a radioactivity count of the operative field to ensure full removal in dubious cases. The removed specimen was sent for a frozen section pathologic examination to ascertain the presence, size and weight of the removed enlarged parathyroid.

Rapid intraoperative PTH assay was used only in the first 12 cases of our series and was abandoned due to the high cost:added value ratio. The wound was closed without drainage and the patients were discharged either the same day or one day after surgery. Postoperative follow-up consisted of serum calcium measurements 8 hours and 24 hours after surgery and an outpatient clinic follow-up visit at 3 and 6 months.

### Statistical analysis

All data were processed using SAS PC software package (SAS Institute, Carey, NC, USA). Comparison of pre- and postoperative values of calcium, phosphorous and PTH were performed using Student's *t*-test.

Tc-99m-MIBI = Tc-99m sestamibi

## Results

Twenty-three operations were performed in 22 patients. The female to male ratio was 13:9, and the mean age  $76.3 \pm 5.9$  years (range 70–88 years). Preoperative mean serum calcium, phosphorus and PTH levels were  $11.7 \pm 1.3$  mg/dl,  $2.5 \pm 0.5$  mg/dl and  $161 \pm 75.4$  pg/ml respectively.

Associated morbidity included one or more of the following: ischemic heart disease (n=15), state after mitral valve replacement (n=1), hypertension (n=22), non-insulin-dependent diabetes mellitus (n=9), chronic obstructive pulmonary disease (n=3), and previous neck surgery for thyroid disease (n=3).

The most common indication for surgery was the presence of hypercalcemia associated with significant depletion of bone mass (n=14), followed by general muscular weakness (n=5), cognitive disorders (n=2) and nephrolithiasis (n=1). In three patients serum calcium levels (<13.0 mg/dl), despite additional manifestations of hyperparathyroidism, constituted the indication for surgery.

### Localization studies predictive value

Agreement between SPECT scan and ultrasonography was observed in 20 patients (90.9%). In two patients there was a disparity between scan and sonographic finding in terms of the site of the adenoma (n=1) and negative sonography (n=1).

### Surgical results

In 20 of the 22 patients the adenoma was found at the predicted site (90.1%). In two patients (9.1%), both with discordant results in the localization studies, no adenoma was found. In one patient a normal parathyroid was biopsied and in the second no parathyroid was found. One of the patients became normocalcemic following surgery without apparent reason. It is noteworthy that both patients were among the first to be operated on with this method.

One patient with histologically proven adenoma found at the predicted site remained hypercalcemic and was re-operated after 2 weeks to find and remove an additional adenoma, on the same side but near the opposite thyroid pole. Mean operation time was  $55 \pm 22$  minutes (including time of frozen section), range 26–85 minutes. The mean size of adenomas was  $1.32 \pm 0.8$  cm in its largest diameter. Mean weight was  $1,334 \pm 2176$  mg.

Immediate (8 hours) mean postoperative serum calcium level was  $9.6 \pm 1.2$  mg/dl (mean  $\Delta$  calcium 2.1 mg/dl,  $P = 0.02$ ). Mean serum calcium, phosphorus and PTH levels at 3 months following surgery were  $9.7 \pm 1.3$  mg/dl ( $P = 0.01$ ),  $3.02 \pm 0.51$  mg/dl and  $35.2 \pm 24.4$  pg/ml ( $P = 0.005$ ), respectively. Twenty-one patients remained normocalcemic at the end of a minimum 6 month period following the operation, mean follow-up being  $17.7 \pm 9.6$  months.

## Discussion

There is little doubt that the treatment modality of choice for PHPT (except in a select group of patients) is surgical removal of the diseased gland/s [10]. The incidence of PHPT in the general population is estimated at 1 or more per 1,000 [11,12], and among older women it appears to be in excess of 1% [13,14]. The ever-increasing proportion of elderly patients in western societies, coupled with the relatively high incidence of PHPT in older

individuals, highlight the importance of this problem. Since PHPT in the elderly is commonly associated with co-morbid conditions, elderly patients are often denied the benefit of surgical treatment for hyperparathyroidism [1,15]. However, with the introduction of new techniques for the localization of the affected parathyroid gland/s [4–6,16] and with the prevailing trend of minimally invasive surgery, several authors have reported unilateral and focused neck explorations for parathyroid adenoma [6,7,17,18], and limited surgery for hyperparathyroidism in the elderly has become a feasible option. Although the consensus developed by the U.S. National Institutes of Health regarding the indications for surgery in patients with PHPT suggested that not all patients over 50 years should undergo parathyroidectomy [19], since there are often ill-defined manifestations of PHPT in the elderly that may broaden the indications for surgery. For example, general muscular weakness, malaise and varying degrees of cognitive disorders, although not directly related to the severity of hypercalcemia, have been shown to improve following parathyroidectomy [8,20]. The indications for surgery in the present series were largely measurable and included mainly severe depletion of bone mass, nephrolithiasis and hypercalcemia exceeding 13 mg/dl. Less quantitatively measurable indications included general muscular weakness and cognitive disorders. Nevertheless, since almost all patients in this series (20 out of 22) had significant associated systemic co-morbidity, they were referred specifically for minimally invasive surgery. Indeed, all patients tolerated the procedure well and there were no deaths or complications related to the patients' associated co-morbidity.

The ability of the sestamibi scan to predict the precise site of the adenoma was 90%. In one case the adenoma was found but the scan failed to detect an additional adenoma. The combined predictive value of scintigraphy and sonography is higher, standing at 95%. Although our numbers are too small to draw a meaningful conclusion, failure to identify the adenoma was directly correlated to disagreement between sonography and scan. Additionally, as the surgical team's confidence and experience increased with this procedure, and patient selection for minimally invasive parathyroidectomy was based on concurrent findings of sonography and sestamibi SPECT scintigraphy, no more failures to identify and remove the adenoma were encountered. As a result of our growing experience with this procedure (>140 cases) we have abandoned the rapid intraoperative PTH assay. The success rate of focused parathyroidectomy with concurring sonography, scintiscan and operative finding with respect to missed adenoma exceeds 95%. This success rate was recently reported with the use of preoperative localization by sestamibi SPECT scintigraphy and intraoperative PTH monitoring [21].

We suggest, based on the results of this series, that focused, minimally invasive parathyroidectomy in the elderly is a safe, well-tolerated and effective procedure. Appropriate patient selection, agreement between two localization techniques and a critical mass of surgical expertise following the unavoidable "learning curve" will ensure a high success rate in curing the elderly patients with PHPT who were once denied surgery.

## References

1. Irvin GL 3rd, Carnerio DM. "Limited" parathyroidectomy in geriatric patients. *Ann Surg* 2001;233(5):612–16.
2. Hindie E, Melliere D, Jeangillame C, Urena P, deLarionle-Vaylet C, Perlmutter L. Unilateral surgery for primary hyperparathyroidism on the basis of technetium-99m sestamibi and iodine-123 subtraction scanning. *Arch Surg* 2000;135:1462–8.
3. Ryan JA, Eisenberger B, Pado KM, Lee F. Efficacy of selective unilateral exploration in hyperparathyroidism based on localization tests. *Arch Surg* 1997;132:886–91.
4. Takami H. Surgical management of hyperparathyroidism in view of a reliable parathyroid adenoma localization test. *Surgery* 1997;120:120.
5. Chen H, Sokkol LJ, Udelsman R. SPECT localization, cervical block anesthesia and intraoperative parathyroid hormone assay. *Surgery* 1999;126(6):1016–21.
6. Norman J, Cheda H, Farrel C. Minimally invasive parathyroidectomy for primary hyperparathyroidism: decreasing operative time and potential complications while improving cosmetic results. *Am Surg* 1998;64(5):391–5.
7. Udelsman R, Donovan PI, Sokkol LJ. One hundred consecutive minimally invasive parathyroid explorations. *Ann Surg* 2000;232:331–9.
8. Heath DA, Wright AD, Barnes AD, Oates GD, Dorricott NJ. Surgical treatment of primary hyperparathyroidism in the elderly. *Br Med J* 1980;280(6229):1406–8.
9. Chen H, Parkerson S, Udelsman R. Parathyroidectomy in the elderly: do the benefits outweigh the risks? *World J Surg* 1998;22(6):531–5.
10. Silverberg SJ, Bilezikian JP, Bone HG, Talpos GB, Hoewitz MJ, Stewart AF. Therapeutic controversies in primary hyperparathyroidism. *J Clin Endocrinol Metab* 1999;84(7):2275–85.
11. Melton 3rd LJ. Epidemiology of primary hyperparathyroidism. *J Bone Miner Dis* 1991;6(2):25–30.
12. Boonstra CE, Jackson CE. Serum calcium survey for hyperparathyroidism: results in 50,000 clinic patients. *Am J Clin Pathol* 1971;55:523–6.
13. Tibblin S, Palsson M, Rydberg J. Hyperparathyroidism in the elderly. *Ann Surg* 1983;197(2):135–8.
14. Lundgren E, Rastad J, Thruftell E, Ackerstom G, Ljunghall S. Population based screening for primary hyperparathyroidism with serum calcium and parathyroid hormone values in menopausal women. *Surgery* 1997;121(3):287–94.
15. Chigot JP, Menegaux F, Achrafi H. Should primary hyperparathyroidism be treated surgically in elderly patients older than 75 years? *Surgery* 1995;117(4):397–401.
16. Civelek AC, Ozalp E, Donovan P, Udelsman R. Prospective evaluation of delayed technetium-99m SPECT scintigraphy for preoperative localization of primary hyperparathyroidism. *Surgery* 2002;131(2):149–57.
17. Reeve TS, Babidge WJ, Parkyn RF, et al. Minimally invasive surgery for primary hyperparathyroidism: systematic review. *Arch Surg* 2000;135(4):481–7.
18. Norman J, Denham D. Minimally invasive radioguided parathyroidectomy in the reoperative neck. *Surgery* 1998;124(6):1088–92.
19. NIH conference. Diagnosis and Management of Asymptomatic Primary Hyperparathyroidism: Consensus Development Conference Statement. *Ann Intern Med* 1991;114(7):593–7.
20. Emmelot-Vonk MH, Samson MM, Raymakers JA. Cognitive deterioration in elderly due to primary hyperparathyroidism-resolved by parathyroidectomy. *Ned Tijdschr Geneesk* 2001;145(41):1961–4.
21. Perrier ND, Ituarte HGP, Morita E, et al. Parathyroid surgery: separating promise from reality. *J Clin Endocrinol Metab* 2002;87(3):1024–29.

**Correspondence:** Dr. M. Shabtai, Dept. of Surgery and Transplantation, Sheba Medical Center, Tel Hashomer 52621, Israel.

Phone: (972-3) 530-2258

Fax: (972-3) 534-1097

email: mshabtai@post.tau.ac.il