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Original Article

Minimally invasive parathyroidectomy in a community based teaching hospital: The role of dual-phase parathyroid scintigraphy and surgeon experience

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Abstract

Aim: In a community based teaching hospital setting, to explore role of dual-phase parathyroid scintigraphy and surgeon experience in minimally invasive parathyroidectomy.

Material and Methods: During 4-year period, from January 2013 to December 2016, 136 of 170 patients those were diagnosed with primary hyperparathyroidism were selected for this retrospective study. For detection of hyper-functioning parathyroid tissue, routine neck ultrasound and 99mTc-MIBI dual phase parathyroid scintigraphy were performed. All scintigraphy scans were evaluated by nuclear medicine physicians and surgeons together. Patients with suspected multiglandular diseases and familial cases were excluded. Enlarged glands were identified by surgeons intraoperatively. Specimens were sent for frozen section analysis.

Results: Without using intraoperative parathormone monitoring or gamma probe, combination of neck ultrasound, surgeon-nuclear physician evaluated parathyroid scintigraphy scan and resection of surgeon-identified diseased gland resulted in 100% cure rate for this group of patients.

Conclusion: Operative experience of surgeon and review of preoperative parathyroid scintigraphy scan had remarkable impact on outcomes. Minimally invasive parathyroidectomy can be held successfully at community-based hospitals under specific conditions without using intraoperative parathormone or gamma probe.

Keywords: Hyperparathyroidism; minimally invasive; surgeon; community; sestamibi; hospital.

INTRODUCTION

Since the first parathyroidectomy operation by Felix Mandl in 1925, diagnosis and surgical management of primary hyperparathyroidism (pHPT) have been changed radically (1). With the introduction of serum autoanalyzer in 1960s, incidence of hyperparathyroidism has started to increase and asymptomatic patients have become very prevalent (2). For the past 25 years, more minimally invasive and selective surgical managements have been the followed trends in pHPT as in all kinds of surgery. Because of that, accurate preoperative localization is essential and further advances have included mostly preoperative localization and special intraoperative techniques such as single-photon emission computed tomography (SPECT), venous sampling of parathormone (PTH), 3-dimensional computed tomography, [11C]-methionine positron-emission tomography, magnetic resonance imaging, rapid intraoperative PTH monitoring (IOPM) and gamma probe (3). Yet, these modern modalities are either expensive or not available in many centers. Most widely used imaging techniques neck ultrasound (US), technetium-99m sestamibi (99mTc-MIBI) scintigraphy, and operative experience of surgeon still play significant role in parathyroid surgery at community-based hospitals (4-6).

On account of that, in this retrospective study, we wanted to evaluate safety and efficacy of surgeon experience in minimally invasive parathyroidectomy (MIP) and productivity of 99mTc-MIBI scan adjunct to neck ultrasound (US) for the evaluation of pHPT prior to surgery.

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MATERIAL and METHODS

This retrospective study was conducted with XXX Research Ethics Committee approval at XXX Hospital which is a community-based teaching hospital. During 4-year period, from January 2013 to December 2016, a total of 170 patients admitted to surgical outpatient clinic for hypercalcemia. For detection of hyper-functioning parathyroid tissue, routine neck ultrasound and 99mTc-MIBI scan were performed. Neck ultrasounds were carried out by miscellaneous sonographers with different technical expertise. Due to experience level of the individual performing US is a limitation, after US, dual phase parathyroid scintigraphy was performed acquiring images at 15, 90 and 180 minutes after the injection of 15 millicurie (mCi) 99mTc-MIBI. All scintigraphy scans were evaluated by nuclear medicine physicians and surgeons together. Initial decision on localization was recorded for all cases. A positive study was defined as description of an abnormal gland in an anatomic quadrant. If a study missed abnormal gland, it was accepted as negative. Serum parathormone (PTH) -second generation immunoassay for PTH-, total serum calcium (Ca++), 25-hydroxyvitamin D (25(OH)D), estimated glomerular filtration rate and bone mineral density were measured preoperatively. After thorough evaluation, 5 patients were found to have secondary hyperparathyroidism, 2 patients tertiary disease and 10 patients had multiglandular pHPT. Patients with suspected multiglandular diseases and familial cases were excluded. 136 patients diagnosed with pHPT were selected for this retrospective study. All of the patients consented to participate in this study. While 62 (45%) patients were diagnosed at surgical outpatient clinic, 72 (52%) patients were referred by endocrinologists, 2 (3%) patients whom had persistent pHPT by other surgeons. Asymptomatic patients were selected for surgery according to the Third International Workshop on the Management of pHPT Guidelines (7).

We adopted MIP using focused lateral approach as a standard procedure for pHPT under general anesthesia (8). Shortly, for a superior parathyroid adenoma, a 2 cm lateral incision to target neck, 1 cm superior to neck crease line, lying lateral to medial margin of sternomastoid muscle and for an inferior parathyroid adenoma, a 2 cm lateral incision to target neck, 1 cm inferior to neck crease line, medial to medial margin of sternomastoid muscle were made according to preoperative imaging studies. If the preoperative localization tests were controversial or abnormal gland couldn't be located during surgery, bilateral neck was explored through a collar incision.

Enlarged glands were identified by surgeons. Specimens were sent for frozen section analysis during surgery and after histological confirmation of parathyroid tissue, operation was terminated. For each patient, operation times -including frozen section analysis- were recorded from the beginning of skin incision until skin closure. Resection of the gland in combination with final histopathological evaluation was considered as the gold standard diagnosis. Early postoperative 6th hour PTH and Ca++ levels were checked out routinely. Clear liquid diet was started at the postoperative sixth hour, and patients were discharged at postoperative 1st day with oral Ca++ supplements in case of low postoperative serum calcium. All patients were followed up for persistent hyperparathyroidism and hypocalcaemia. Surgery was accepted as successful after 6 months of normocalcaemia.

Statistical analysis was performed using SPSS 20.0 software (SPSS Inc., Chicago, IL, USA). All data were checked for normality and homogeneity before the statistical analysis. Data showing normal distribution were expressed as mean ± standard deviation, if otherwise median values were used. Wilcoxon test was used for pairwise comparison. P value of 0.05 was accepted statistically significant.

RESULTS

Our study consisted of 136 patients with a median age of 58 years. While most of the patients were asymptomatic, most common symptom was bone/joint pain followed by nephrolithiasis. The most common accompanying disease was hypertension followed by diabetes mellitus. Elevated PTH and Ca++ levels were present in all cases. The median preoperative PTH level was 232 pg/mL, the median preoperative serum Ca++ 11.5 mg/dL and the mean lumbar T score -2.1(±1.1).

Table 1. Demographic and laboratory data of patients

Variable		Results
Age, y, median (min-max)		58 (20-84)
Gender, n (%)		
	male	16 (11.8)
	female	120 (88.2)
Symptoms, n (%)		
	asymptomatic	66 (48.5)
	bone/joint pain	51 (37.5)
	nephrolithiasis	14 (10.3)
	neuropsychiatric	1 (0.7)
	fragility fracture	2 (1.5)
Additional diseases, n (%)		
	hypertension	43 (31.6)
	diabetes mellitus	14 (10.3)
	asthma	6 (4.4)
	chronic kidney disease	6 (4.4)
	rheumatoid arthritis	2 (1.5)
	none	65 (47.8)
Imaging size**, mm, median (min-max)		18 (6-60)
Multinodular goiter, n (%)		77 (56.6)
Bone mineral density at lumbar spine, t-score. Mean±SD		-2.1±1.1
Type of operation, n (%)		
		124 (91.2)
		10 (7.4)
		2 (1.5)
Location, n (%)		
	right upper pole	11 (8.1)
	right lower pole	62 (45.6)
	left upper pole	8 (5.9)
	left lower pole	52 (38.2)
	intrathyroidal	3 (2.2)

Table 2. Summary of preoperative localization tests.	
Positive Neck US, n (%)	65 (47.8)
Positive ^{99m}Tc-MIBI, n (%)	127 (93.4)
Neck US and ^{99m}Tc-MIBI concordant, n (%)	64 (47.1)
Neck US and ^{99m}Tc-MIBI discordant, n (%)	4 (2.9)
Accurate localization to anatomic quadrant for neck US, n (%)	61 (93)
Accurate localization to anatomic quadrant for ^{99m}Tc-MIBI, n (%)	127 (100)
Sensitivity of neck US	46.21
Sensitivity of ^{99m}Tc-MIBI	93.38

Table 3. Laboratory results			
Variable	Preoperative	Postoperative	P value
Parathormone, pg/ml, median (IQR)	232 (227)	12.3 (28)	<0.001
Calcium^{++}, mg/dl, median (min-max)	11.5 (10.1-16.1)	9.6 (6.9-11.7)	<0.001

Neck ultrasound identified parathyroid adenoma in 61 (44.8%) cases precisely, in 71 (52.2%) cases it was inconclusive. 99mTc-MIBI planar scan was accurate in 127 (93.4%) cases and negative only in 9 (6.6%) cases. Sensitivity for US was 46.21%, for 99mTc-MIBI planar scan 93.38%. Both US and Scintigraphy were negative in 7 cases (Table 1).

Of 136 patients, in 7 (6.6%) patients with negative preoperative localization tests, 2 patients with persistent pHPT and 1 patient with discordant preoperative localization test, bilateral neck was explored for diseased gland. In 2 (1.5%) patients, minimally invasive surgery was converted to traditional neck incision due to intrathyroidal parathyroid gland and ipsilateral lobectomy was performed. In 124 (91.9) patients minimally invasive parathyroidectomy was performed. Of 124, in 3 patients with discordant findings, after analysis of preoperative images with nuclear medicine physicians and radiologists, minimally invasive surgery was conducted (Table 2).

The final pathology was single parathyroid adenoma in 133 (97.9%) patients, parathyroid neoplasia in 2 (1.5%) patients and parathyroid carcinoma in 1 (0.7%) patient. The median operation time for minimally invasive surgery was 75 minutes (range 40-180 min), for bilateral neck exploration 125 minutes (range 80-220 min) ($p<0.01$). In cases with converted surgery, it was 145 minutes. The most common location for parathyroid adenoma was right lower pole (45.6%) followed by left lower pole (38.2%). In 2 referred patients with persistent pHPT, missed glands were found in previously explored anatomic location. The mean length of stay in minimally invasive surgery group was 19±3.2 hours and for bilateral neck exploration group, it was 20±3.5 hours. But we couldn't find statistical significance between them ($p>0.05$).

Early Postoperative 6th hour PTH and Ca levels (reference ranges for PTH and Serum Ca++ in the laboratory, 12-88 pg/mL, and 8.4-10.2 mg/dL, respectively) returned to normal range in 100 (73.5%) patients. While in remaining 36 patients (26.5%), long-term follow up at a median of 7.3 months (range 6-14) showed normal PTH and Ca levels. Although patients with low postoperative serum calcium were discharged with oral Ca++ supplements, 9 (6.6%) patients required additional hospitalization due to symptomatic hypocalcaemia. No other complication was observed. Cure rate was 100% for both minimally invasive surgery and bilateral neck exploration. (Table 3).

DISCUSSION

Preoperative imaging methods and intraoperative parathormone monitoring are the debate topics in the recent studies assessing surgical treatment of pHPT (9-11). Yet, there is no consensus on which imaging method is superior or which threshold to use during IOPM (11-16). While in most suburban and community hospitals, surgeons keep performing minimally invasive parathyroidectomy under neck US and 99mTc-MIBI parathyroid scintigraphy guidance (17, 18). In this study, minimally invasive parathyroidectomy results of a community-based hospitalin which nearly 30 parathyroidectomies per year are performed- was represented and it demonstrated that without IOPM or gamma probe, high sensitivity of 99mTc-MIBI planar scan and operative experience of surgeon plays a crucial role in highly successful cure rates. Intraoperative adjunct techniques do not seem to be a necessity especially when performed at community-based hospitals by surgeons who preserved their skills by regularly carrying out MIP (19, 20).

Surgery is gold standard and it is the only curative treatment in pHPT (7). Only two decades ago, bilateral neck exploration was the choice of surgery and minimally invasive surgery for parathyroid adenoma was anathema to endocrine surgeons (21). With the guide of modern equipment in the late 1990s, preoperative localization of diseased glands became possible and the need for bilateral exploration was questioned. Furthermore, advances in preoperative localization techniques allowed smaller incisions and general term "Minimally Invasive Parathyroidectomy" has been used to cover these unilateral approaches. Compared to bilateral neck exploration, less complication rates, shorter operation times and better cosmetic results were reported after (22). We have adopted MIP using focused lateral approach in a similar fashion to Smit et al. and Agarwal et al. (8, 23). In our center, neck US and 99mTc-MIBI parathyroid scintigraphy are available for localization of enlarged parathyroid gland. Despite limitation, MIP has been performed at this center in the majority of the patients by mostly relying on these preoperative methods and operative experience of surgeon.

Preoperative localization results highlighted that neck US and parathyroid scintigraphy was concordant in 47.1% of the cases which was lower than previously reported. In the studies of Paravastu et al., Mihai et al. and McVeigh et al., results of compatible findings were 60%, 57% and 52%,

respectively (6, 24, 25). Prager et al. reported negative impact of thyroid pathology on the results of neck US in an endemic region (26). So that reduced sensitivity of neck US was attributed to concurrent presence of thyroid nodules, which were fit to be followed conservatively, in 56% of the patients. It should be also noted that Kayseri province is an endemic goiter region (27). In contrast, accuracy of preoperative scintigraphy to predict anatomic location was 100%. In their research, Krausz and friends reported concomitant thyroid nodules decreased positive predictive value of MIBI scintigraphy (28). We believe interpretation of scans with nuclear radiologists increased the chance of preoperative localization in the present study. In their work, Zia and colleagues also recommended interpretation of scintigraphy results by surgeons rather than relying on radiological report (29). Combination of neck US, surgeon-nuclear physician evaluated 99mTc-MIBI parathyroid scintigraphy scan and resection of surgeon-identified diseased gland resulted in 100% cure rate for this group of patients.

In the literature, presence of second adenoma in patients with pPHT varies from 4% to 13% and, IOPM has been regarded as a valuable tool to alert surgeon for an additional diseased gland during surgery (30). In the Suliburk et. al.'s 10-year cohort, 0.9% of the patients were found to have double adenomas and they stated that even with a strict threshold for IOPM, 0.45% of the second adenomas, which is immensely low, could not be diagnosed intraoperatively. However, in patients with hyperplasia, IOPM could be a valuable adjunct method. But, considering reported prevalence of multiple gland hyperplasia is 5.74% and for double adenomas 4.14%, the real question should be "Does IOPM add value to decision making process" (31). In the cost analysis model of Morris et. al., IOPM was found to incur 4% additional cost and, if the probability of cure without IOPM exceeds %98, using IOPM is never a cost saving strategy (32).

There are several other factors described in the literature affecting surgical outcome. Researchers have been exploring correlation between hospital/surgeon volume and post-operative outcome. In a recent study, strong relation was found between increasing operative volume and improved outcomes in a procedure specific genre (33). Maruthappu and his friends systematically reviewed studies assessing the influence of surgical experience and noted that with increased volume and years of experience comes improved outcome (34). This affect was well described in surgery for hyperparathyroidism (35, 36). Chen and colleagues stated that in high volume centers those had parathyroidectomy were less likely to have missed gland in anatomic location than undergoing parathyroidectomy at low volume centers (37). Although annual case load used to describe high volume differs in the literature, this study was conducted at a medium-volume community hospital (38). In the current study, re-operative parathyroidectomy was performed in 2 patients due to persistent disease. Clinical approach to re-operative operation was same as initial surgery. Missed glands were found in their previously explored quadrant. We were also able to achieve a 100% success rate for those. As Udelsman and associates indicated, most of the re-operative parathyroidectomy can be avoided if initial surgery is conducted by experienced surgeons (39). Since delineation of experienced surgeon is vague, we believe the term should be based on regular conduction of a specific procedure.

CONCLUSION

In conclusion, minimally invasive procedure allowed rapid recovery and patient comfort. Not only operative experience of surgeon but also review of preoperative 99mTc-MIBI parathyroid scintigraphy scan had remarkable impact on outcomes where advanced pre/intra-operative adjunct methods are not available. Apart from this study, minimally invasive parathyroidectomy can be held successfully at community-based hospitals under specific conditions. Newly described pre/intra-operative methods may aid inexperienced endocrine surgeons in dealing with parathyroid adenoma and can be preserved for re-operative parathyroid surgery.

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