Radio-guided minimally invasive parathyroidectomy under local anesthesia

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Summary

Background: **Despite the high success rate of the complete bilateral neck exploration to treat primary hyperparathyroidism, less invasive alternatives have been emerging. In an attempt to reduce operative time and decrease perioperative morbidity, we reported our experience with radio-guided minimally invasive parathyroidectomy (RMIP) under local anesthesia.**

Study design: **A retrospective chart review was carried out to study 55 consecutive patients, in an adult tertiary care hospital (Montreal General Hospital), who underwent RMIP under local anesthesia over a 30-month period. Charts were reviewed for operative information, radiological and pathological diagnoses and post-operative course. The main outcome measures were the accuracy of localizing the parathyroid adenoma, operative time, achievement of normocalcemia post-operatively and perioperative morbidity.**

Results: **Of the 55 patients we studied, 51 were cured as defined by normocalcemia following a single intervention, for an overall cure rate of ~ 93%. Four patients required an additional procedure: In two because of failure to remove a diseased gland, and in two because of multiglandular disease. The preoperative sestamibi scan accurately predicted the location of all abnormal parathyroid glands in 53 cases. In the remaining two cases, the scan failed to predict multiglandular disease. Average total operative time was 39 minutes. There were no major complications.**

Conclusions: **RMIP under local anesthesia is a safe and effective modality to treat primary hyperparathyroidism. The short operative time, the use of local anesthesia and the low complication rate make this technique a viable alternative.**

Key-words: ***Technetium-99-sestamibi scan, Hyperparathyroidism, Parathyroid adenoma, Parathyroidectomy, Local anesthesia.***

Résumé

Introduction: En dépit d'un taux élevé d'exploration coplete du cou bilatéral pour la prise en charge d'hyperparathyroidisme primaire connu du succès, des alternatives moins invasifs se faire jour. En essayant de faire baisser la durée opératoire et diminuer la morbidité périopératoire, nous venons de rapporter notre expérience en ce qui est du guide par radio de la parathyroidectomie invasive minimale guidée par radio (PIMR) sous l'anesthésis locale.

Plan d'étude: Un bilan retrospectif graphique a été effectué afin d'etudier 55 patients consécutifs, dans un hôpital des soins tertiaire pour des adultes (Hôpital Général du Montreal), qui ont subi, PIMR sous l'anesthésie locale au cours d'une période de 30 mois. Des diagrammes ont été passé en revu pour des informations opératoire, des diagnostics pathologiques et radiologiques es évolution post opératoire. Les demarches majeures pour les résultats étaient l'exactitude de la localisation d'adénorme parathyroide, temps d'opération, etaient l'exactitude de la localisation d'adenorme parathyroide, temps d'operation, les succes de la normocalcémie post opératoire et la morbidité périopératoire.

Résultats: Parmi les 55 patients étudiés, 51 ont été soignés comme defini par la normocalcémie à la suite d'une seule intervention, indiquant, dans l'ensemble, le taux de guérison de -93%. Quatre patients exigent des protocols supplémentaires, chez deux patients a cause de l'insuccès d'enlever une glande malade et dans deux cas, à cause de la maladie multiglandulaire. : l'examen au scanneur sestamibi préopératoire a correctement prédit le siège de toutes des glandes parathyroides anormales chez 53 des cas. Dans les deux autres cas, le scanneur n'arrive pas à predire la maladie multiglandulaire. Temps opératoire moyen était 39 minutes. Il n'y avait aucun cas de la complication majeur.

Conclusion: Le PMR sous l'anesthésie locale est une méthode sans danger et efficace pour la prise en charge d'hyperparathyroidisme primaire. Le temps opératoire bref, l'utilisation d'anesthésie locale, et la diminution dans le taux de la complication permit cette méthode d'etre acceptée comme un alternatif viable.

Introduction

Primary hyperparathyroidism is a disorder that occurs in about 25 per 100,000 of the general population. Approximately 85% of cases are due to parathyroid adenoma, 12% are due to hyperplasia, and the rest are due to double adenomata, or rarely, parathyroid carcinoma.[1] The classic operation for primary hyperparathyroidism consists of bilateral neck exploration, complete evaluation of all parathyroid glands, and removal of a solitary adenoma or partial resection of the hyperplastic parathyroid glands. Despite the high cure rate (>95%) of this procedure, if performed by an experienced surgeon,[2-5] different approaches have been tried to decrease operative time, length of hospital stay as well as perioperative morbidity while maintaining an excellent outcome.

In 1989, Coakley et al reported a new approach using the technetium Tc 99m-sestamibi scan for routine preoperative parathyroid localization.[6] Subsequently, several studies have reported that this nuclear medicine scan can identify solitary parathyroid adenoma with high success rate.[7-13] Recently, with the use of radio-guided surgery with gamma probe and intraoperative parathyroid hormone assay, several investigators have reported high success rates with reduction in operative time and length of hospital stay.[14-21] However, similar results have not been reported by others. For example,

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Burkey et al reported that directed parathyroidectomy utilizing the gamma probe or intact parathormone levels (iPTH) does not significantly alter the operating time, length of hospitalization, cure rate, morbidity, mortality, or patient satisfaction when compared to conventional exploration.[22] We think that our study is important because it will attempt to address this controversial issue.

The gamma probe is a small handheld device that can be used during the operation to localize radioactivity. Following the injection of technetium Tc 99m- sestamibi preoperatively, it will be selectively taken up by abnormal parathyroid glands and subsequently localized by the gamma probe. Thus, gamma probe could help in limiting the field of dissection and hence, shortening the surgical time.

In this report, we describe our results in 55 consecutive patients who underwent radio-guided minimally invasive parathyroidectomy (RMIP) under local anesthesia with the use of preoperative technetium Tc 99m-sestamibi scan, gamma probe intraoperatively, and frozen-section confirmation of tissue diagnosis.

Patients and methods

We conducted a retrospective chart review of 55 consecutive patients who underwent parathyroid exploration with the aid of gamma probe by one endocrine surgeon at the Montreal General Hospital between June 1999 and November 2001. All patients were included for analysis. All patients were diagnosed with primary hyperparathyroidism based on their elevated serum calcium and iPTH. One patient had previous neck exploration for a removal of parathyroid adenoma.

Preoperatively, all patients underwent technetium Tc 99m sestamibi scanning as outpatients. Patients were injected with 20 mCi technetium Tc 99m-sestamibi. Early and delayed scans were performed 10 minutes and 3 hours after injection, respectively. All scans included anterior-posterior and oblique views. Scans interpretations were done by a board certified nuclear medicine radiologist indicating the expected location of an adenoma. The operating surgeon was notified about the result of each scan and noted that in his preoperative or operative note or both in all cases. If patients with hyperparathyroidism did not have a positive preoperative sestamibi scan, they were not included in this study.

On the day of surgery, each patient received a second injection with 30 mCi technetium Tc 99m-sestamibi two hours before his or her operation. In the operating room, intravenous Meperidine and Diazepam were given for sedation. Patient's head was kept in the neutral position and on occasions we asked the patient to extend chin. All four quadrants of the neck were scanned with a handheld gamma counter (Navigator, US Surgical Corp., Norwalk, CN). Incision was placed according to the expected location of the adenoma as determined by both sestamibi scanning and by placement of the gamma probe over the skin to detect the highest site of radioactivity. The chosen site was then injected with 10cc of 1% Xylocaine and epinephrine to achieve local anesthesia. A 2 cm transverse skin incision was made, and subsequent dissection was guided by placing the gamma probe in the wound to localize the highest source of radioactivity. After identifying an adenoma, it was removed and checked for degree of radioactivity ex vivo. A strongly positive scan is highly suggestive of a parathyroid adenoma. The removed specimen was then sent for frozen pathological evaluation. If the frozen-section analysis confirms the diagnosis of parathyroid tissue, the operation would conclude. To close, strap muscles were approximated at midline, and skin was closed with a running subcuticular stitch. All cases were performed by the same endocrine surgeon (R.T.) with the assistance of a surgical resident or a medical student. Total operative time was measured starting at the time of incision and ending at the placement of the dressing.

Patients were kept in the recovery room for 1 hour, and then admitted to the surgical ward and monitored for vital signs, neck hematoma, voice changes, and symptoms of hypocalcaemia. The patients were discharged the day after surgery, after verifying the appropriate decrease in the serum calcium levels.

Statistical analysis

All quantitative data are expressed as mean $\pm$ standard error of the mean. Statistical analysis was performed using an unpaired Student's t-test and P value less than 0.05 were considered significant.

Results

Our series included 44 women (mean age 62.8 years [range19 to93]) and 11 men (mean age 50.5 years [range 23 to71]). At the time of surgery, 22 patients (40%) were older than 65 years of age. Symptoms associated with hyperparathyroidism in our patients are shown in Table 1. The mean preoperative ionized calcium level was 1.58 ± 0.05 mmol/l (normal 1.15 to 1.32 mmol/l) and the mean preoperative iPTH level was 25.43 ± 3.28 pmol/l (normal 1.6 to 6.9 pmol/l).

Of the 55 patients described here, 51 underwent successful RMIP under local anesthesia and intravenous sedation with retrieval of a diseased parathyroid and subsequent normalization of serum calcium. In the remaining 4 patients, 2 required subsequent conversion to open neck exploration under general anesthesia because of failure to retrieve a diseased gland as a result of operative difficulties either due to an enlarged goiter or short neck with kyphoscoliosis. The other two patients continued to have elevated ionized serum calcium and iPTH levels postoperatively, and a second adenoma was discovered in both of them on subsequent scanning. They required a second RMIP to remove the second adenoma and achieve normocalcemia.

Sestamibi scanning was performed in all 55 patients. Results and actual scans were available in the operating room. The preoperative sestamibi scan accurately predicted the location of all abnormal parathyroid glands in 53 cases. In two patients, the scan failed to predict multiglandular disease as

Table 1 Symptoms associated with hyperparathyroidism

Recurrent kidney stones	19 (34%)
Bone pain or osteopenia	18 (33%)
Hypercalcemic crisis	1 (2%)
Peptic ulcer disease	1 (2%)
None	16 (29%)

described above.

Although we were not planning to identify the recurrent laryngeal nerve, we were able to localize the nerve in approximately one third of our patients. Three patients developed hoarseness during their operations; however, this completely recovered by the end of the operation.

Our average operative time to remove a single parathyroid adenoma was 39 minutes, which included 10 to 15 minutes waiting for the frozen-section results. Patients in our study were sent home the day following the surgery. This allowed us to monitor them for possible surgical complications. All patients were discharged as planned with no surgical morbidities.

Patients' average postoperative ionized calcium level was 1.27 $\pm$ 0.02 mmol/l and their mean preoperative iPTH level was 8.14 $\pm$ 0.71 pmol/l. Both of these were significantly lower than preoperative values ($P<0.001$). The average follow-up period was 5.5 months (range, 1-39 months). During the follow up period, no surgical related morbidities were identified in any of our patients.

Therefore, of the 55 patients we studied, 51 were cured as defined by normocalcemia following a single intervention, for an overall cure rate of ~ 93%. Four patients required an additional procedure: In two because of failure to remove a diseased gland due to operative difficulties, and in the remaining two patients because of multiglandular disease.

Discussion

Although the standard four gland exploration has excellent cure rates and minimal morbidity, the need for less invasive procedures with lower risk and more convenience, while maintaining the same cure rates, is growing. Several reports have examined the combination of preoperative technetium Tc 99m sestamibi localization with the use of gamma probe intraoperatively.[14-18] These reports suggested that gamma probe is a useful tool which, if combined with preoperative technetium study, allows for accurate and rapid identification of parathyroid adenoma.

In our study, preoperative sestamibi scanning were accurate, with only two false- negative findings (sensitivity 96%), which is comparable to the results of other centers.[13, 23-25] The use of gamma probe allows the surgeon to confirm the preoperative scan results and to focus the dissection on the radioactive adenoma. Norman and Chheda have shown that parathyroidectomy could be done with a smaller incision if gamma probe is used.[16] Norman and Denham demonstrated that the use of gamma probe technique is efficacious in patients with hyperparathyroidism who have undergone previous neck exploration for parathyroid or thyroid disease.[17] With the help of this technique, they were able to perform the same minimally invasive surgery that they used in previously unoperated neck.

We scanned all the removed specimens with the gamma probe away from the operative field to compare their radioactivity with that of the background. A strongly positive scan is highly suggestive of a parathyroid adenoma. All specimens in the present study were sent for frozen-section analysis to confirm the diagnosis of parathyroid tissue. Murphy and Norman studied 345 patients who underwent radio-guided parathyroidectomy.[26] They measured the ex vivo radioactivity in parathyroid and other tissues within 3.5 hours of sestamibi injection. Background radioactivity was measured after tissue excision, and ratios were calculated. They reported that lymph nodes, normal parathyroids, and fat never contained more than 2.2% of background radioactivity, whereas parathyroid adenomas were reported to contain 59% +/- 9% of background radioactivity (ranging from 18% to 136%). They concluded that any excised tissue containing more than 20% of background radioactivity, in a patient with a positive sestamibi scan, is a solitary parathyroid adenoma. Sullivan et al reported their experience with the gamma probe for rapid intraoperative localization of parathyroid adenomas.[19] They scanned all removed specimens off the operative field, and found that a strongly positive scan was consistent with the specimen being a parathyroid gland. However, they recommended that a parathyroid surgeon should use either intraoperative parathyroid hormone levels or frozen-section analysis of a normal appearing gland to rule out four-gland hyperplasia. In our present report, we used frozen-section to confirm the diagnosis of parathyroid tissue in the removed specimen.

Our average operative time of 39 minutes is comparable to those of other surgeons.[20,21] We believe that we have not surrendered operative accuracy to reduce operative time because our 93% accuracy is comparable to the 95% rates reported by surgeons performing the standard four-gland exploration. However, our success rate could have been better had we used intraoperative parathyroid hormone level determination. Our series does not represent a random sampling of patients with primary hyperparathyroidism. Only about 70% of our patients with primary hyperparathyroidism had positive sestamibi scans and therefore could be offered this procedure.

Conclusions

If appropriately selected, most patients with primary hyperparathyroidism can be treated successfully with the combination of preoperative technetium Tc 99m sestamibi localization and the use of the gamma probe intraoperatively. The short operative time, the use of local anesthesia and the low complication rate make this technique a viable alternative, especially in elderly patients with comorbidities. The success of this approach depends largely on the accurate interpretation of high-quality sestamibi scans.

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