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Research Article

Success of Minimally Invasive Parathyroidectomy Despite Negative Sestamibi Scan

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Abstract

Objective: Evaluate minimally invasive parathyroidectomy in patients with primary hyperparathyroidism and negative Sestamibi scan results.

Methods: A retrospective review was performed from July 2003 to July 2010 of patients with primary hyperparathyroidism and negative Sestamibi scan results. All patients were treated at a tertiary academic center and the senior author performed all parathyroidectomy. 38 patients were included. No patients were excluded. Results of preoperative Sestamibi scans and ultrasound were reviewed. Operative reports, pathologic diagnoses, and postoperative reports were reviewed.

Results: Of the 38 patients with negative Sestamibi scans, 33 (86%) had positive ultrasound findings, which focused the area of surgery. Of the 33 patients with positive ultrasound findings, 28 patients (85%) underwent minimally invasive parathyroidectomy for a single adenoma with successful surgical cure. The 5 remaining patients had double adenomas or parathyroid hyperplasia. Of the 5 patients with negative Sestamibi scans and negative ultrasounds, 3 were found to have single gland disease, which was surgically cured.

Conclusion: A negative Sestamibi scan does not preclude a minimally invasive neck exploration to cure primary hyperparathyroidism. With adjunctive ultrasound, a majority of patients may undergo minimally invasive parathyroidectomy with surgical success.

Keywords: Parathyroidectomy; Sestamibi; Hyperparathyroidism; Parathyroid

Introduction

Parathyroidectomy is first line therapy for patients with primary hyperparathyroidism. In the majority of cases of primary hyperparathyroidism, disease is due to single gland disease, or parathyroid adenoma. In these patients, the treatment of choice is excision of the single involved parathyroid gland [1-13].

There is an overall trend toward minimally invasive parathyroid surgery by those who routinely operate on parathyroid glands [2]. Historically, patients with primary hyperparathyroidism underwent bilateral neck exploration for identification and removal of the affected gland(s) [1]; however with the incorporation of specialized imaging for localizing the pathologic gland to a specific quadrant of the neck, the surgeon is able to plan and execute a more precise operation. Minimally invasive parathyroid surgery indicates a focused neck exploration that is limited to a unilateral neck exploration that is guided by pre-operative imaging and the success of the procedure is determined by intra-operative biochemical testing (rapid PTH). The majority of endocrine surgeons who perform these minimally invasive parathyroid surgeries utilize focused small (central or lateral) incisions as well as intraoperative rapid PTH assays for biochemical confirmation [2]. The ability to use a focused incision and limit dissection depends on reliable localization imaging to provide accurate representation of the adenoma relative to its surrounding anatomy. The standard for preoperative parathyroid adenoma localization has been the 99mTc-Sestamibi scan and when results clearly demonstrate localization to a single quadrant, the study is highly useful to the surgeon [3]. In these cases, minimally invasive parathyroidectomy has a high success rate [4].

However, difficulty arises when the Sestamibi scan fails to localize a pathologic parathyroid gland. Negative Sestamibi scan results have been associated with higher rates of multiglandular disease5 as well as lower rates of biochemical cure (as defined by postoperative lab studies of calcium and parathyroid hormone levels) [3].

The objective of this study was to evaluate whether minimally invasive parathyroidectomy can be successful in patients with primary hyperparathyroidism who have nonlocalizing (or negative) Sestamibi scans by using cervical ultrasound to localize the involved parathyroid glands.

Materials and Methods

Approval for this study was obtained from the Institutional Review Board at the University of Texas Health Science Center at San Antonio. This study employed a retrospective review of medical records of patients treated by the senior author at our tertiary academic referral center from July 2003 to July 2010. The study population included patients referred to our institution for surgical evaluation of primary hyperparathyroidism that also had negative Sestamibi scans.

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All patients with a negative Sestamibi scan subsequently underwent cervical ultrasound imaging as part of preoperative planning. Patients were then taken to the operating room, where successful parathyroidectomy was confirmed with use of intraoperative rapid Parathyroid Hormone (PTH) assay. Our criteria for biochemical cure of the hyperparathyroidism at the time of surgery included intact PTH levels that decrease by more than 50% and fall into the normal range from the highest pre-incision or pre-excisional hormone levels in a peripheral blood sample obtained 10-15 minutes after the removal of abnormal parathyroid tissue [14]. The inclusion criteria for these patients required that patients have 1) diagnosis of primary hyperparathyroidism, and 2) negative Sestamibi scan results. No patients were excluded from this study.

A retrospective review of these patients' records was conducted, including review of preoperative imaging studies, operative reports, and final pathology reports.

Results

Thirty-eight patients with primary hyperparathyroidism and a negative Sestamibi scan underwent additional imaging with cervical thyroid ultrasound. Of the 38 patients with negative Sestamibi scans, 33 (86%) had ultrasound findings that allowed localization for focused surgery. Of these 33 patients with localizing ultrasound findings, 28 (85%) underwent minimally invasive parathyroidectomy for a single adenoma with a successful surgical cure. The remaining 5 patients had either double adenomas (3 patients), or multigland disease (2 with parathyroid hyperplasia).

There were 5 patients (14%) in this study who were found to have both negative Sestamibi and negative ultrasound results. Ultimately, 3 were found to have single adenoma and 2 patients demonstrated multi-gland disease at the time of surgery. All 38 patients in this population underwent successful parathyroidectomy with surgical cure, as confirmed by intra-operative PTH levels after removal of the pathologic gland(s). Long term follow-up (> 6 months) was available for 35 of the 38 patients. Of those 35 patients the long term cure rate (normal calcium and normal intact PTH) was 32/35 (92%). The mean long term follow-up in this patient population was 19.2 months (range 6 to 32months). In the 3 patients with recurrence of hyperparathyroidism 2 patients are being observed with mildly elevated Calcium and PTH. One patient` underwent re-exploration with removal of second adenoma.

These results demonstrate that ultrasound imaging in the setting of a negative Sestamibi scan has a sensitivity of 90% and a specificity of 29% for localizing parathyroid adenoma prior to parathyroidectomy. According to our study, the Positive Predictive Value (PPV) of ultrasound localization for single gland parathyroid disease when Sestamibi scan is negative is 85%, whereas the Negative Predictive Value (NPV) is only 40%.

Discussion

Parathyroidectomy is commonly performed in patients with primary hyperparathyroidism. A recent review demonstrated that the overall number of parathyroid surgeries performed worldwide has increased dramatically over the 20 year span from 1980 to 2000 [2]. The same authors performed a survey of endocrine surgeons and found that over half of these surgeons who perform parathyroidectomy do so using a minimally invasive technique [2]. Minimally invasive parathyroidectomy has decreased morbidity due to decrease operative times, limited dissection, and decreased hospital stay [2]. The ability to perform focused surgeries depends heavily on localizing imaging studies, like Sestamibi scans, which have been used with success since the concept of minimally invasive parathyroidectomy was introduced [6]. Additional imaging studies have also been examined and have been found to be especially useful in cases where a Sestamibi scan does not provide localizing information. The negative Sestamibi parathyroid scan is felt to be more likely in patients with smaller volume parathyroid pathology, in patients with multi-nodular goiters, and in patients with potential ectopic parathyroid glands. In our study, as in other similar studies, ultrasonography is a useful adjunct for correctly identifying single gland disease in patients with negative Sestamibi scans [3]. Ultrasound is a very useful tool when used in the setting of a negative Sestamibi, as illustrated by the high percentage of positive ultrasounds in our population [4]. In our study, ultrasound imaging was performed by our institution's radiology department; however use of in-office ultrasound performed by the clinician at the time of evaluation adds an additional component for consideration. A study by Adler et al. found that surgeon-performed ultrasound was more successful in localizing additional pathologic glands when compared to radiology-performed ultrasound [4].

This study demonstrated the utility of ultrasound imaging in cases of negative Sestamibi scans for patients undergoing preoperative planning for parathyroidectomy. Ultrasonography in the setting of negative Sestamibi scan has a high sensitivity for localizing single-gland disease and good positive predictive value for obtaining surgical cure. In fact, a large majority of our patients in this study had a positive ultrasound, which allowed for successful execution of minimally invasive parathyroidectomy. In those patients who did not have localizing ultrasound imaging studies, successful surgical cure was achieved with standard bilateral neck exploration and parathyroidectomy. This number is small (26%) in comparison to the total number of negative Sestamibi scans. The low number of bilateral neck explorations for parathyroidectomy observed in this study for patients with primary hyperparathyroidism and a negative Sestamibi scan can be attributed to the successful localization of single-gland disease provided by ultrasonography.

With respect to alternative methods of imaging in patients with primary hyperparathyroidism, the use of 4-dimensional CT scanning has become a useful method for evaluating parathyroidectomy patients preoperatively. The 4-D CT scan has been used in combination with ultrasound as a protocol for preoperative localization with good sensitivity and specificity (82% and 93% respectively) [7]. Beland et al. also demonstrated that 4-D CT has high sensitivity and specificity (82% and 92%) for localizing occult parathyroid adenomas when either prior surgery attempts or localization studies with ultrasound and Sestamibi were unsuccessful [8]. The 4-D CT scan has thus been demonstrated to be an accurate method for localization, and some even advocate its exclusive use for preoperative imaging in lieu of ultrasound and/or Sestamibi scan [9]. On a similar note, a recent JAMA Surgery article also described using contrasted neck CT scans to create 3-dimensional video models that could be used for preoperative planning as well as intraoperative augmentation where

images could be projected into the surgical field for parathyroid surgery [10].

Limitations to the routine use of preoperative CT scans include the concern for increased radiation exposure as well as significant increased cost of 4-D CT scanning compared to standard Sestamibi scan [4]. A Sestamibi scan causes several times less radiation exposure compared to CT scanning [7]. In fact, one study found that the radiation dose to the thyroid caused by 4D-CT scanning was about 57 times greater compared to the traditional Sestamibi scan [11]. When combined with CT scanning (conventional CT or SPECT), however, the cost of combined CT-Sestamibi scan is comparable to 4D-Computed Tomgraphy.4 While 4D-CT has become a popular imaging alternative, it must be considered in the light of contrast exposure, radiation exposure, cost to the patient, and overall accessibility to the imaging modality [9,11,4]. Clearly, preoperative imaging remains a vital and evolving component of surgical planning in parathyroidectomy.

An additional consideration for the use of cervical ultrasonography in the context of primary hyperparathyroidism is the possibility of discovering concurrent thyroid disease. Ultrasound in this area is often the first test performed for suspected thyroid pathology and as such, would be a useful evaluation in a patient already planning for a surgery in the same anatomic region. Discovery of concurrent thyroid disease could potentially allow for preoperative planning, prevention of repeat surgery, and optimization of resources if a thyroidectomy incision was planned at the onset [12].

Regardless of the imaging method or methods used, localizing imaging remains a critical component of the appropriate preoperative workup for potential candidates of parathyroidectomy. Radiographic studies can provide useful information for surgical decision-making regarding minimally invasive technique, as well as highlight any relevant anatomy or adjacent pathology. In our institution, a positive Sestamibi scan is invaluable for preoperative planning for minimally invasive parathyroidectomy, while a negative scan is somewhat problematic. In the majority of those cases, we have been able to successfully utilize adjunct cervical ultrasonography to localize single-gland parathyroid disease and perform minimally invasive parathyroidectomy without the need for significant added cost or radiation exposure. There will always be a small portion of patients with primary hyperparathyroidism who have multi-gland disease, and as such, will be unable to undergo minimally invasive parathyroid surgery. In these cases, bilateral neck exploration will be necessary, and as demonstrated in our study as well as others, these patients often have negative ultrasound imaging in the setting of a negative Sestamibi scan. The key to treating this patient population is to perform adequate neck exploration and to confirm post-excision reduction in PTH using intraoperative assays and/or postoperative follow up labs (calcium, PTH), as this group of patients with 'dual-negative' imaging has a high postoperative failure rate (as indicated by persistent disease) [13].

Our findings also suggest that an algorithm could be developed for preoperative imaging in patients with primary hyperparathyroidism. In our study, Sestamibi followed by cervical ultrasound was able to accurately localize parathyroid pathology in the majority of patients; however, as discussed above, there is also a role for 4D CT scanning in these patients.

Limitations of this study include relatively small sample size. However, our study evaluated a sample size similar to a subset studied in other evaluations of negative Sestamibi results [3]. This study is also limited by the retrospective nature of project and the inherent need for accurate documentation in order to review records after the fact.

Conclusion

Negative Sestamibi scan does not preclude successful minimally invasive parathyroidectomy. Ultrasound is a useful adjunct in these cases.

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