Improvement of minimally invasive parathyroidectomy outcomes by real time ultrasonography performed by a surgeon and radiologist team.

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Abstract

Aims: Minimally invasive parathyroidectomy (MIP) has become the first line of treatment for primary hyperparathyroidism caused by solitary parathyroid adenoma. In order to increase the sensitivity of high-resolution ultrasonography (hUS), surgeon performed ultrasonography (SUS) has been increasingly used preoperatively. However, a radiologist and surgeon performing ultrasonography (RSUS) has not been a usual practice. In this study, we aimed to evaluate the clinical contribution of RSUS on MIP. **Material and methods:** From 2012 to 2014, a total of 30 consecutive patients (4 male, 26 female, mean age 48.87±14.52 years) with solitary parathyroid adenoma, were included in the study. All patients underwent preoperative hUS and Technetium-99m sestamibi scintigraphy. In patients, demographic characteristics, diagnostic tools used, levels of biochemical parameters, duration of operation, and length of hospital stay were recorded. **Results:** Adenomas were successfully localized by US in all patients and the surgical approach was determined according to this localization. Parathyroidectomy with MIP was successfully performed under local anesthesia in all patients. Mean operation time was 19.87±3.35 min. Post-operative PTH and calcium values were significantly decreased. All patients were discharged from the hospital in the same day. None of the patients had complications such as recurrent laryngeal nerve injury, hematoma, or injury to nearby organs. None of the patients had drains placed. **Conclusions:** Adenoma is well localized by US and thus, MIP can be completed under local anesthesia. US provides a very important clinical contribution to the success of MIP. In addition to these, RSUS helps in determining the location of the incision and the shortest way to achieve the lesion; therefore, it provides a small incision and shortens duration of the operation with a minimal dissection.

Keywords: parathyroid adenoma, ultrasound, preoperative procedure, minimal access parathyroidectomy

Introduction

The incidence of primary hyperparathyroidism (pHPT) is increasing and is currently estimated to occur in 1:500 women and 1:2,000 men [1]. The traditional surgical approach is the bilateral neck exploration of all four parathyroid glands [2-4] with success rates exceeding 95% and minimal morbidity [2,5]. However, pHPT is caused by a solitary adenoma in 85-90% of patients

[2,6,7]. With developing technologies such as parathyroid Technetium-99 m sestamibi scintigraphy (SS) and high-resolution ultrasonography (hUS), minimally invasive parathyroidectomy (MIP) seems to be the first choice.

MIP can be defined as the ability of the surgeon to perform traditional surgical procedures in novel ways to minimize the trauma of the surgical exposure [8,9]. Given the safety and high success rate of bilateral neck exploration, the potential advantages of MIP are: decreased operating times (OT), decreased hospitalization time, reduced level of physical invasiveness, and better cosmetic results [8]. However, the success of MIP depends on accurate preoperative localization of parathyroid adenomas [10-12].

hUS and SS are currently the most widely used preoperative localization modalities. The sensitivity of hUS

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and SS identification of parathyroid adenomas ranges between 70% and 90% [4,13,14]. Although the sensitivity of hUS and SS are high for solitary parathyroid adenomas, negative results of imaging studies are inevitable [4,15,16]. hUS is favored because of its low cost, convenience, lack of radiation exposure, and ability to evaluate concomitant thyroid nodules; however, it may fail to detect ectopic parathyroid adenomas [4,14,17]. Also, it has the disadvantage of being operator-dependent, with sensitivities ranging from 20% to 79% among sonographers, depending on skill, experience, and interest [18-20]. In order to increase the sensitivity of hUS, surgeon-performed ultrasonography (SUS) has been increasingly used preoperatively, and has been shown to be highly accurate in localizing abnormal glands [21-24]. However, to the best of our knowledge, the effectiveness of radiologist and surgeon performed ultrasonography (RSUS) before MIP has not been evaluated in any studies yet.

In this study, we aim to evaluate the effect of RSUS on the success rate of finding adenoma, operating time, conversion to the general anesthesia, and complications.

Material and methods

From January 2012 to October 2014, a total of 98 consecutive patients were operated at Dicle University for pHPT. In 30 patients the pHPT was caused by solitary parathyroid adenoma and these patients were included in the study. All the patients had biochemically confirmed pHPT and single gland disease supported by imaging methods such as SS and hUS. Positive results seen on imaging modalities was used for the selection of glands to be excised. Parathyroidectomy with local anesthesia and intravenous sedation for well-localized solitary gland was preferred for patients who had no contraindication for intravenous sedation. Exclusion criteria were suspicion of multiple gland disease, multiple endocrine neoplasm syndrome or parathyroid carcinoma, non-cooperative patients who were requesting general anesthesia and preoperatively diagnosed intrathyroidal parathyroid (fig 1a) or thyroid disease requiring thyroidectomy. No intraoperative parathyroid hormone assay was used after excision of the gland. All excised glands weight and sizes were measured after removal. All removed specimens were fixed in a 10% formalin solution and sent to pathology. In this study frozen section was not used and operation was finalized after excision of the gland. Biochemical values of all patients were recorded. Parathyroid hormone (PTH), total serum calcium phosphor levels of all patients were measured preoperatively. These levels were measured

again postoperatively in the first day, 2nd week, 3rd month, and 6th month.

The demographic characteristics of the patients, operation time (OT), and hospitalization time were retrospectively recorded from the hospital database.

Ultrasound technique

Combined RSUS (RUS + SUS) took place in the presence of both (surgeon + radiologist) in the Radiology Department, one day before surgery. Patients were scanned in supine position with neck in hyperextension. A complete cervical ultrasound with imaging of the thyroid, parathyroid glands, vascular structures, and any associated lymphadenopathy was documented. The incision site was determined and marked under US guidance. The anatomic location and dimensions of suspected abnormal parathyroid glands were recorded.

Anesthetic technique

Intravenous 0.02 mg/kg midazolam was given in the preoperative room then patients were moved into the operation theatre and 1 µg/kg fentanyl IV was given after monitorization. A mixture of 1 mg/kg 0.25 % bupivacaine and 1 mg/kg 1 % lidocaine was prepared and half of the dose was used on the incision area. The other half was used for the infiltration of the deeper levels and neighboring tissues. If patients complained of pain, the sedation of the patient was increased with 0.5 mg/kg propofol. If by any reason conversion to general anesthesia was required the patients were intubated by the anesthesiologists.

Surgical technique

MIP was performed through a 3-3.5 cm curvilinear transverse collar incision approximately 2-3 cm above the sternal notch. We used two different approaches (anterior or lateral approach) in operations, whichever is appropriate (fig 1b). The type of approach was decided before with RSUS (fig 1c, d). In the anterior approach or midline approach, the plane between the strap muscles was used. In the lateral approach, or back-door approach, the plane between the strap muscles medially and the carotid sheath laterally was used. Operation time was defined as the duration from the incision made and up to stitching of the skin.

Statistical analyses

Statistical analyses were performed using SPSS software program version 15.0 for Windows (SPSS Inc., Chicago, IL, USA). Categorical variables were expressed as counts and percentages, while continuous variables were expressed as mean ± standard deviation or range. Differences between baseline and postoperative Ca, P and PTH values were tested using paired samples t-test or Wilcoxon rank test after determining normality according to Kolmogorov-Smirnov test. A p value <0.05 was considered statistically significant.

Fig 1. a) Round hypoechoic parathyroid adenoma completely surrounded by the right lobe of the thyroid, which is not suitable for minimally invasive parathyroidectomy; b) Approaches to Parathyroid Gland. Two incision types used for minimally invasive parathyroidectomy (A – Incision for lateral approach, B – Incision for medial approach, C – Sternal notch, D – Midline, E – Anterior border of sternocleidomastoid muscle); c) Parathyroid adenoma adjacent to lateral of trachea and posterior aspect of the inferior portion of right lobe of thyroid gland, which is proper for anterior approach; d) Parathyroid adenoma anterior to common carotid artery and internal jugular vein, posterior to the left lobe of thyroid gland, which is proper for lateral approach. C – Arteria carotis communis, PA – Parathyroid adenoma, T – Thyroid gland, Tr – Trachea, VJI – Vena jugularis interna

Results

Of the 30 patients, 26 (86.7%) were female. The average age of the patients was 48.87 ± 14.52 years (range 19-75). The distribution of excised adenomas was 63.3% (n=19) in the right side and 36.7% (n=11) in the left side. Intervention with local anesthesia was applied to all patients. There was no patients with body mass index (BMI) higher than 30. None of the patients required conversion to general anesthesia.

All patients had biochemically confirmed pHPT and single gland disease supported by imaging methods, SS and/or hUS. hUS and SS were performed in all patients. While parathyroid adenomas were detected with hUS in all patients, SS was unable to identify parathyroid adenoma in two (6.7%) patients. According to hUS and operative findings, localization of parathyroid adenomas was 18 (60.0%) in right lower zone, 1 (3.3%) in right upper zone, 9 (30.0%) in left lower zone, and 2 (6.7%) in left upper zone. All adenomas detected with SS were in concordance with hUS and operation localization.

The average weight in excised parathyroid adenomas was 3.44 ± 4.43 gr (range 0.5-17.6 gr), while the average of the largest diameter was 2.08 ± 0.99 cm (range 0.8-4.5 cm). Preoperative and postoperative mean serum total

calcium, phosphorus, and PTH values are detailed in table I. While postoperative Ca and PTH levels were significantly lower than preoperative values ($p < 0.001$), the phosphorus value was significantly higher ($p = 0.015$).

All patients were followed-up for at least 6 months. According to biochemical results (serum PTH, total calcium and serum phosphorus), cure was achieved in all patients. This indicates a successful operation.

Mean operation time was 19.87 ± 3.35 min (range 15-28 min).

All patients were discharged from the hospital or transferred to the Endocrinology Department in the same day.

None of the patients had complications such as recurrent laryngeal nerve injury, hematoma, or injury to nearby organs.

Discussions

The technical success rate of MIP was 98% in the study of Udelsman [25]. This rate reached 100% in our study. The normalization of calcium levels in parathyroid surgery shows the success of the operation. But it should not be considered as the single indicator of the success. Surgery should also be performed with minimal morbid-

Table I. Biochemical results of patients.

Parameters	Preoperative	Postoperative 1st day	Postoperative 6th month	Normal range
PTH	749.22 ± 998.04	24.31 ± 15.47	56.73 ± 17.26	15-65 pg/ml
Calcium	11.91 ± 1.89	8.51 ± 0.91	9.13 ± 0.89	8.4-10.2 mg/dl
Phosphor	2.50 ± 0.67	2.88 ± 0.67	3.60 ± 0.61	3.2-5.5 mg/dl

PTH: Parathyroid hormone

ity, no mortality, low recurrence rates, and a reasonable cost [26]. MIP prevents unnecessary mobilization of neck structures, thereby lowering the rate of recurrent laryngeal nerve damage [25,27]. The solitary adenoma causes 85–90% of all pHPT [27–29]. For single gland disease, MIP can be applied securely and efficiently with local anesthesia and intravenous (IV) sedation [30–33]. In a large number of centers, MIP can now be routinely performed as an outpatient procedure [25,34–37]. However, it can be sufficient if accurate preoperative localization is performed [2,3,6,38,39]. The combination of SS and neck hUS has a 74–90% sensitivity in localizing a parathyroid adenoma [18,19,40,41].

Nowadays, hUS is increasingly being used. Performing a hUS before the patient undergoes MIP is beneficial as it enables exact localization of the pathologic parathyroid. It is highly sensitive in detecting parathyroid adenomas located behind the thyroid gland or beyond the lower contour of the thyroid. It also enables the identification and evaluation of any concomitant thyroid disease prior to surgery. Recently, SUS has been increasingly used as a complementary imaging study to SS [42–44]. It has shown that SUS is as good as RUS in localizing single gland disease in patients with sporadic pHPT. The sensitivity of SUS in localizing parathyroid adenomas has been reported to be 67%–87% [18,22,45–47]. Steward et al [46] reported one of the highest success rates for SUS: a sensitivity of 91%. The rate of accuracy results of previous studies are detailed in Table II.

When US is performed by the operating surgeon it allows the surgeon to directly visualize the parathyroid adenoma and take real-time images, in multiple planes, in the preoperative setting and correlate it with the thyroid and other landmarks in the neck. [42]. Also, it permits

the planning of the neck incision, thereby increasing the safety of the operation [52]. Therefore, we think that the time spent for surgery following RSUS is shorter than that for surgery following RUS, showing that combination of the surgery with RSUS is effective. In patients with morbid obesity, surgical procedure is much more challenging in terms of operation time, length of incision, seroma, drainage. In our study, all patients had BMI under 30.

Radiologist's role cannot be denied in detecting parathyroid adenoma. For example, in one case the adenoma within carotid sheath was not determined by SUS, but was easily found with RUS. In this study, we showed that when an experienced radiologist, along with a surgeon, perform US preoperatively, solitary adenomas in all the patients were found easily and accurately. It is important to have an available radiologist on site and demand. There is a learning curve associated with SUS. Arora et al [48] mentioned that they confirmed their SUS with MIBI for the first 250 patients, to complete the learning curve. In our method we think that only ten cases are enough for a learning curve, because we perform US in the presence of a radiologist, not a surgeon alone. While MIP was completed successfully in 84% of patients (under local anesthesia) in one study [31], the completion rate was 100% for us. One should consider that proper patient selection and the experience of the surgical team play an important role in the conversion rate. This characteristic explains in part the very low conversion rate reported in larger series (0.9–8%) [53,54]. In our study we have no case requiring conversion to general anesthesia, due to the proper selection of the cases.

While Kwon et al [2], determined the localization of parathyroid tumor by examining preoperative documents,

Table II. Comparison of success of localization methods in primary hyperparathyroidism.

Author	Year	n	Method (the success rate)			
			RUS n(%)	SUS n(%)	SS n(%)	US+SS n(%)
Soon et al [18]	2008	218	148(82.76)	87(81.76)		
Deutmeyer et al [21]	2011	220		96(88)		
Aliyev et al [24]	2014	1000		842(84)	842(82.5)	
Gilat et al [27]	2004	77	77(85.72)			
Teksoz et al [30]	2013	42	15(35.71)		11(26.9)	16(38.09)
Untch et al [42]	2011	516	503(76)	392(87)		
Steward et al [46]	2006	106	106(42)	106(82)	106(44)	
Jabiev et al [47]	2009	442		52(88.5)		390(74.9)
Arora et al [48]	2009	160		160(74)	119(56)	
Livingston et al [49]	2008	100		18(94)	79(79)	
Hughes et al [50]	2014	1910		1644(80)	1165(88)	920(88)
Prasannan et al [51]	2007	130		103(79.2)	102(78.4)	

RUS: radiologist performed ultrasonography, SUS:surgeon-performed ultrasound, SS: technetium-99m sestamibi scintigraphy, US: ultrasonography. n: the number of patients

we evaluate this in real-time. While radiologists perform hUS in the supine position, radiologists and surgeons perform hUS in supine position with hyperextension which is the position used in surgery. This position provides the surgeon the location of the adenoma and its relation to neighboring structures such as surrounding vasculature and the trachea. It also provides the nearest incision localization and distance from skin to adenoma. This leads to less tissue damage and a shorter operation time. Anatomical localization facilitates skin incision placement by the lateral mini-incision technique and improves cosmetic results [2,5]. MIP are carried out through a 2–4 cm incision [8,34].

Deutmeyer et al [21] performed operations under general anesthesia by intraoperative PTH monitoring based on SUS localization and showed that SS adds little additional information to guide surgery. Some authors do not advocate MIP with hUS as the only preoperative investigation study because the size of a parathyroid gland does not correlate with the function [18,55]. Using hUS localization alone, it is therefore possible to remove an enlarged nonfunctioning parathyroid gland and miss the smaller pathological gland [18]. However, in our study, SS could not detect adenoma in two patients and it did not provide additional information to hUS in our other patients. Therefore, we suggest using SS only for the cases with unclear hUS findings. In this situation the radiation exposure is avoided and can save money and time.

Black et al [56] suggested that although local/cervical block anesthesia and general anesthesia groups were equivalent for experienced complications, the advantage of local/cervical block anesthesia vs general anesthesia relates to the decreased operating time, costs, and need for oral pain medication. Compared to general anesthesia, local anesthesia [57] and hypnosedation [58] decrease rates of nausea and vomiting, resulting in decreased postoperative bleeding. Additionally, endotracheal intubation by itself has been associated with objective functional voice changes in as much as 5% of patients [59]. On the contrary, several studies show that general anesthesia give more comfort for surgeon while dissecting the tissues, leading to a reduced risk of hemorrhage [59,60]. Local anesthesia and hypnosedation is especially appropriate for ASA III or IV anesthetic risk category [8]. Furthermore, avoidance of general anesthesia and/or a hospital admission for the vast majority of patients results in significant cost savings.

A focused anterior approach, which is the most commonly used technique for MIP, includes lateral retraction or sometimes splitting of the strap muscles. Many studies about MIP mention the anterior approach [30-32]. In the lateral approach the gland is reached by splicing the

anterior wall of the sternocleidomastoid muscle and lateral border of the strap muscles via a small skin incision [30,33]. In this study, we think that decision of surgical approaches (anterior or lateral) by RSUS provided an important benefit in duration and feasibility of the surgery.

MIP shortens the operative and anesthesia time [27,29,61]. In literature the mean operation time of MIP ranges from 15 to 56 minutes [30,31]. It also shortens the hospitalization time [25]. In this study, duration of the surgery was short (~20 min) and patients were not hospitalized longer than one day.

There are several limitations to this study. First, the ultrasonographers, both radiologists and surgeons, were not blinded to the results of SS. Second, this was a retrospective study that did not have a control group. A larger study (necessarily randomized, multicentric) would be better in order to assess the results after RUS (branch 1), SUS (branch 2) and RSUS (branch 3). Finally, the small number of patients that were enrolled in the study was a limitation.

Conclusions

The success of MIP depends on the success in localization and identification of abnormal glands. In MIP, the incision is small, dissection is minimal, postoperative pain is less, and hospital stay is shorter. These procedures may be done as an outpatient surgery, even with local anesthesia. As a result, it is important that surgeons join hUS, due to the selection of patient and successful treatment of selected patients. We think that surgeons and radiologists are complementary to each other. Moreover, our success which was 100%, stems from RSUS. If patients require a second operation, the anatomical structures of the region will be intact. Use of local anesthesia avoids complications associated with general anesthesia.

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