

A new technique to simplify the minimally invasive parathyroidectomy: Ultrasound-assisted guided wire localization for solitary parathyroid adenomas

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Abstract

Objective: To investigate the benefits of ultrasound-assisted guided wire localization in MIP for selected cases.

Methods: In this prospective, nonrandomised study, we included 36 patients with solitary parathyroid adenomas diagnosed preoperatively by 99m Tc sesta MIBI scintigraphy and/or neck ultrasonography. An ultrasound-guided wire was placed in the solitary parathyroid adenoma preoperatively. MIPs were performed under local anaesthesia plus sedation. After the excision, the parathyroidectomy was confirmed with postoperative ultrasonography.

Results: There were 36 patients included in our study. The mean age was 54.89±11.28 years, and 30 patients were females (83.3%). Preoperative PTH and calcium (Ca) levels were 269.5 pg/mL (83.5-5,000 pg/mL) and 12.2 mg/dL (11.1-20 mg/dL), respectively. Postoperative serum PTH and Ca levels were 42.04±26.65 pg/mL and 8.95±0.74 mg/dL, respectively. The mean operation time was 21.69±6.4 minutes and the average hospitalisation time was 18 hours (range: 10-72 hours).

Conclusions: Ultrasound-assisted guided wire localization may be useful in selected MIP cases. The MIP advantages include higher success rates and being easy to learn and practise.

Keywords: parathyroid neoplasms, Minimally invasive surgical procedures, Parathyroidectomy, Monitoring, Intraoperative, Ultrasonography. (JPMA 66: 1427; 2016)

Introduction

Primary hyperparathyroidism (pHPT) is characterised by symptomatic hypercalcaemia with high parathyroid hormone (PTH) levels in the absence of secondary or tertiary causes. Bilateral cervical exploration with the identification of the parathyroid glands and the removal of a hyperfunctioning adenoma is the main treatment.¹ Most patients with pHPT have a solitary adenoma and these patients are usually cured when this hyperactive gland is removed. Performing a safe and effective anaesthesia for parathyroid surgery under hypercalcaemic conditions can become a problem for anaesthesiologists.^{2,3} This condition can be dangerous with comorbid diseases including those of the cardiovascular and respiratory systems. Local anaesthetic techniques are safer than general anaesthesia (GA) in these high risk groups.³

In recent years, preoperative and perioperative localization techniques for parathyroid adenomas have

been developed and, for this reason, minimally invasive parathyroidectomies (MIPs), such as video-assisted endoscopic and mini incision parathyroidectomies, have been frequently applied. Preoperative 99m Tc sesta MIBI scintigraphy, intraoperative radio-guided parathyroidectomy, selective use of intraoperative frozen tissue examinations and intraoperative PTH assays play a major role in MIPs.⁴⁻⁸ MIPs have lower surgical and anaesthetic complication rates, with a reduced hospitalization time and cost compared with conventional parathyroidectomies. Additionally, one advantage of this method is the high success rate that varies from 95-100%.⁹ The process used for the MIP intraoperative radio guided parathyroidectomy is expensive and time consuming; moreover, it requires skilled and trained personnel. Procedures are needed that are inexpensive, simpler and require less personnel for MIP. Therefore, we aimed to investigate the benefits of an ultrasound assisted guided wire localization method that is more simple and inexpensive. We aimed to investigate the benefits of ultrasound-assisted guided wire localization in MIP for selected cases.

Methods

Prospective nonrandomised patients (n=36) underwent MIP between March 2013 and November 2014 in Canakkale Onsekiz Mart University Faculty of

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Medicine Hospital General Surgery Clinic. Each participant signed an informed consent form in accordance with the Declaration of Helsinki. This study was approved by the local ethics committee of Canakkale Onsekiz Mart University. Patients with pHPT were included in the study. The pHPT diagnosis was based on persistently high serum calcium (Ca) levels and inappropriately high levels of intact PTH. Preoperative neck ultrasonography (USG) and a ^{99m}Tc sestamibi scintigraphy were performed in all patients. Preoperative patient data including age, sex, serum Ca levels, PTH levels, medical history, imaging studies and operation times were recorded. Patients with a solitary enlarged parathyroid adenoma, which can be observed with a parathyroid ultrasound, were included in our study. Multiple gland parathyroid hyperplasia, previous neck exploration for thyroid or parathyroid diseases, arranged simultaneous thyroid operations for thyroid disorders, allergies to local anaesthetics and the patient's rejection to participate in this study were exclusion criteria.

Surgical failure, conversion to a collar incision, and GA procedures were explained to the patients. Postoperative normocalcemia and decreased PTH levels were accepted as surgical success.

Neck Ultrasonography

Neck USGs were performed with a high resolution, 7.5-12.5 MHz transducer (Logic P5, GE, USA). The parathyroid adenoma was recognized on gray-scale imaging as a hypoechoic nodule. Neck USGs were performed during both the pre- and intraoperative periods for all patients.

Anaesthesia Technique

Oxygen (4 L/min) was administered to all patients. Anaesthesiologists monitored NIBP, ECG, SpO₂. Epinephrine (1/100,000) with lidocaine was injected for the local anaesthesia. We were careful to ensure toxic doses were not administered during the local anaesthesia. We did not perform a cervical block. In case of pain or intolerance to the local anaesthesia, intravenous midazolam, fentanyl citrate and propofol were added for sedation. No patients required GA.

Localization of the parathyroid adenoma

All patients were evaluated with parathyroid scintigraphy and neck USG. Patients with adenomas were operated on when the localization of the parathyroid adenoma was detected with both scintigraphy and a neck USG. Patients with adenomas that were detected by a parathyroid scintigraphy but

not detected with a neck USG were excluded from the study. In certain patients, a parathyroid adenoma could not be detected with parathyroid scintigraphy, however, the adenoma was detected by a neck USG. The levels of PTH washout were examined by needle aspiration biopsies from parathyroid adenomas in these patients.

Surgical Technique

Pre- and peri-operative USGs for both parathyroid localization and confirming its excision were performed on the operating table. Cutaneous and



Figure-1: USG assisted guided wire localization for the parathyroid adenoma.

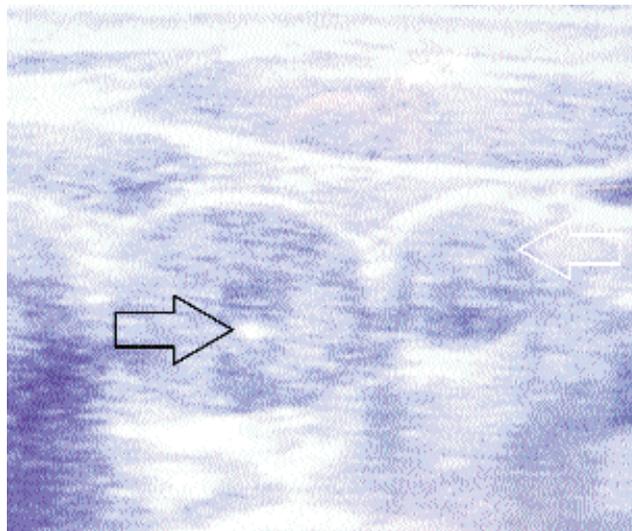


Figure-2A: Preoperative guided wire localized in the left inferior parathyroid adenoma. Black arrow shows the guided wire, White arrow shows the carotid artery.

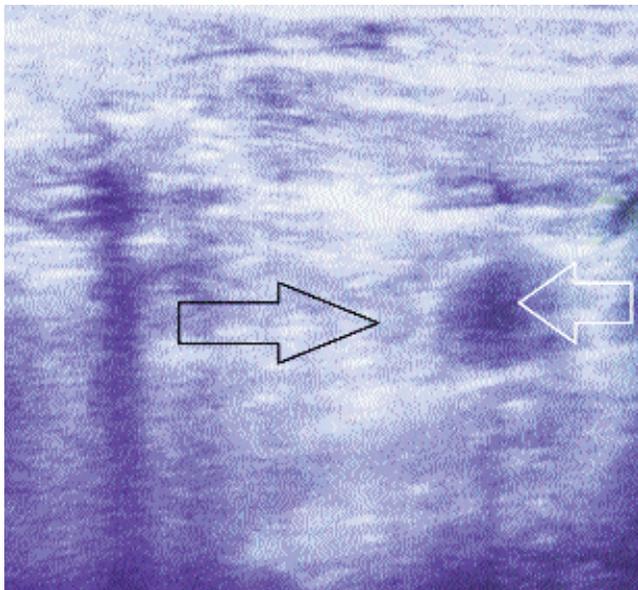


Figure-2B: At the end the excision of the adenoma was confirmed with intraoperative USG. Black arrow shows the excised parathyroid area, white arrow shows the carotid artery.

subcutaneous local anaesthetic material was administered to the incision. We used a percutaneous guided wire in the adenoma under USG assistance (Figure-1), and the wire was inserted into the nodule (Matek® 20G/10 cm breast localization needle-Ankara) (Figure-2). A mini incision of 2-3 cm was made in the dermis and subdermis under the guidance of the wire. The sternocleidomastoid and strap muscles were lateralized. Marked at the tip of the needle, macroscopically different tissue appeared. The parathyroid adenoma was removed together with the wire. At the end of the procedure, the excision of the adenoma was confirmed with an intraoperative USG. When no mass was located in the operative area, the operation was considered finished.

Biochemical Analysis

Serum levels of total and corrected Ca, albumin, intact PTH, creatinine and alkaline phosphatase were evaluated with routine biochemical laboratory tests. The reference range for serum Ca was 8.5-10.2 mg/dL, and the serum Ca levels were corrected with albumin levels (formula: corrected Ca = total Ca + 0.8[4 - albumin]). Intact PTH was measured using an electrochemiluminescence immunoassay on a Roche Cobas e-601 analyzer (Roche Diagnostics GmbH, Mannheim, Germany). The assay reagents were also obtained from Roche Diagnostics, and the reference range used was 15-65 pg/mL.

Statistical Analysis

Statistical analyses were performed using SPSS software (Version 19.0; IBM, Chicago, IL, USA). Continuous variables were expressed as mean \pm SD, and categorical variables were expressed as percentages. For continuous variables, normal distribution was assessed using the Kolmogorov-Smirnov test.

Results

A total 36 MIPs were included in our study. The average age of the patients was 54.89 ± 11.28 years. The patients were predominantly female (83.3%). The demographic properties of the patients are listed in Table. The preoperative median serum PTH and corrected Ca levels were 269.5 pg/mL (83.5-5,000 pg/mL) and 12.2 mg/dL (11.1-20 mg/dL), respectively. Postoperative mean serum PTH and Ca levels were 42.04 ± 26.65 pg/mL and 8.89 ± 0.74 mg/dL, respectively.

Thirty-three (91.7%) parathyroid adenomas were diagnosed with ^{99m}Tc sesta MIBI scintigraphy. Of these, 19 (57.6%) patients were right sided and 14 (42.4%) patients were left sided in the ^{99m}Tc sesta MIBI scintigraphy. All adenomas were seen by USG, which found that 22 (61.1%) patients were right sided and 14 (38.9%) patients were left sided. All adenomas were inferiorly localized. Parathyroid adenomas were not observed with parathyroid scintigraphy in three patients; however, neck USGs confirmed their presence in these patients. Moreover, parathyroid adenomas were verified with fine-needle aspiration biopsies and PTH levels as determined with a washout $> 5,000$ pg/ml in these patients. The operative mean incision length was 2.72 ± 0.64 cm. In five patients (13.9%), incision extensions were required. The mean operation time was 21.69 ± 6.41

Table: Demographics of the study group.

Sex	
Female	30 (83.3%)
Male	6 (16.7%)
Age (years)	54.89 ± 11.28
PTH (pg/mL)	
Pre-op, median	269.5 (range: 83.5-5,000)
Post-op	42.04 ± 26.65
Calcium (mg/dL)	
Pre-op, median	12.2 (range: 11.1-20)
Post-op	8.95 ± 0.74
Localization of the adenoma in the USG	
Right	22 (61.1)
Left	14 (38.9)
Localization of the adenoma in the MIBI	
Right	19 (57.6)
Left	14 (42.4)

minutes and the median hospitalisation time was 18 hours (range: 10-72 hours).

Dislocation of the guided wire was observed in three patients (8.3%). Postoperative complications included haematomas in two patients (5.6%), mild hypocalcaemia in one patient (2.8%) and hoarseness in one patient (2.8%).

Discussion

In recent years, the MIP has become a popular technique in parathyroid surgery. The advantages of this technique include smaller incisions, it can be done with local anaesthesia, there is less tissue trauma, less postoperative pain and shortened hospitalisation times. The success of the MIP surgery is related to correct pre- and perioperative adenoma localization.¹⁰ For various reasons, many surgical and local anaesthetic techniques have been described for MIPs. This study presents a different technique for both the localization of the adenoma and the MIP. It has been shown to be reliable and easily applied for selected cases, with significantly reduced operative times, shorter hospital stays and lower complication rates.

After the first MIP technique, several new minimally invasive surgical techniques have been attempted. Further perioperative USG, perioperative gamma probe use for sesta MIBI imaging, and methylene blue marking methods have been used for localization of adenomas. Additionally, confirmation of a total excision with these techniques includes intraoperative PTH levels and frozen sections.¹¹⁻¹⁵ The aim for all of the studies is based on minimizing costs and maximizing the correct localization. We aimed to standardize the effective intraoperative use of USG and perform a parathyroid adenoma excision with wire guided localization assisted by USG. Preventing the dislocation of the adenoma does not require any radioactive materials or agents, which are the advantages of the wire-guided lumpectomy WGL method. The perioperative use of USG in all stages of the surgery minimized any residual adenoma.

In the literature, CT-assisted guided wire marking is another method for MIP.¹¹ However, this method has been of little interest by clinicians. The disadvantages of this method include a prolonged application time, required intervention outside the operating room, administering radiation to the patient and increased costs. When we compared this method to our technique, we used no radiation and had shorter surgical durations and application times within the operating room, all of which are advantages to our technique. Additionally, the

reduction in patient anxiety has to do with the fact that all procedures occur within the operating room and sedation can be provided in our method.

Scintigraphy is the most commonly used method for preoperative adenoma localization. It is a very effective method to determine tumour localization linked to a parathyroid adenoma. However, for perioperative adenoma localization, some supportive nuclear medicine methods including the use of gamma have been used.^{7,8,16} In parathyroidectomies with a radioactive marked localization using this method, success rates are high. However, the disadvantages of this technique include the high cost of equipment, the use of radioactive materials, the exposure of both patients and operating personnel to radiation and the fact that the gamma probe marking must be performed outside the operating room. Additionally, the necessary equipment and experienced personnel are not widely available in the majority of hospitals, which are the most important barriers for the common use of this technique. No requirement for extra equipment, no radioactive material costs, applicable within the operating room and a lack of radiation are important advantages of our method. Also, it can be applied within the operating room, which allows at least a 30-minute advantage in terms of operating duration compared with the gamma probe. All of these factors allow the possibility of widespread use of our technique.

The most important stage for the success of MIP is determining whether the parathyroid adenoma has been successfully removed. For this stage, the most frequently used method is to check the intraoperative PTH (IPTH) levels and/or pathologic diagnosis with frozen sections.² Additionally, PTH washout can be done from the removed lesion. Previously accepted as the gold standard, checking IPTH and frozen sections have reached high diagnostic accuracy rates in selected endocrine laboratories. However, the macroscopic specimen excised by the surgeon may include some lymph nodes, fat tissue, thymus or thyroid nodules. According to the literature, the false positive rate of frozen sections alone is reported as 6%.^{14,17} This may result in extra costs, loss of time, sometimes even ending in unnecessary dissections. Even if the removed specimens are confirmed as an adenoma by frozen sections, sometimes these cannot provide information about the presence of any residual adenoma. Measurements of the IPTH and frozen sections cause a 10-15-minute extension of the operation time.¹⁸ In our study, after the removal of the parathyroid adenoma, we used an intraoperative USG to check the excision. There have been

no studies concerning the single use of ultrasound for residual tissue after the excision of an adenoma in the recent literature. This method is very simple and can be used intraoperatively. After removing the parathyroid adenoma, we observed that the excision can be confirmed by USG. Compared with intraoperative PTH measurements and analysing frozen sections, our method is faster and cheaper than the other methods. However, to show the effectiveness of this method, a larger series is required.

Performing an MIP under local anaesthesia, the surgical duration was significantly reduced compared with GA procedures. In fact, the most important factor that extends the duration of parathyroid surgery is the technique for identifying the adenoma, including intraoperative PTH measurements or frozen sections. If the preoperative waiting time for adenoma identification with a gamma probe is excluded, the average duration of the operation is 30 minutes (range: 15-65 minutes). After the excision, the time necessary to take a blood sample, in addition to waiting for the blood results and pathologic confirmation of intraoperative IPTH and/or frozen sections, extends the duration by about 20 minutes. The surgical incision cannot be closed before obtaining blood results and additional doses of local anaesthetics or sedative agents may be required. In our study, the average surgical duration was very short and was significantly lower than the times observed with other techniques.

In our study, guided wire dislocation spotted in three cases, reinsertion was done under USG guided. No patients had a permanent rise in PTH and Ca levels and required a reoperation due to insufficient resection. Postoperative haematomas developed in two cases. USG controls observed that the haematoma did not moderate in one patient and did not require any intervention. The other patients' haematomas drained under USG. No wound infection or seroma formation occurred in our patients. The two patients with haematomas were discharged 24 hours after their operations, and all other patients were discharged at the postoperative 12th hour.

Another important advantage of our method of placing a guided wire under USG is the short duration of the learning curve for both endocrinologists and endocrine surgeons. Especially for surgeons dealing with endocrine surgery, the application and learning of this technique is very simple. There was no significant difference between the success rates of the first application and the later ones. The only parameter that changed between the first patient and the last with this

technique was the duration of the surgery; however, this difference was an acceptable duration of about 8-10 minutes. In our study, we reached a 100% success rate without requiring additional tests like IPTH, gamma probes and frozen sections.

Study Limitations

Having an inadequate patient number was the only limitation of our study. Further studies with larger series and multicentre studies are required.

Conclusion

The MIP is the gold standard treatment method for primary solitary adenomas. Adenoma localization is very important to the success of the MIP. An ultrasound-assisted guided wire may be useful for adenoma localization in selected MIP cases.

Disclosure: No.

Conflict of Interest: No.

Funding Sources: No.

References

- Adil E, Adil T, Fedok F, Kauffman G, Goldenberg D. Minimally invasive radioguided parathyroidectomy performed for primary hyperparathyroidism. *Otolaryngol Head Neck Surg* 2009; 141: 34-8.
- Barczynski M, Konturek A, Cichon S, Hubalewska-Dydejczyk A, Golkowski F, Huszno B. Intraoperative parathyroid hormone assay improves outcomes of minimally invasive parathyroidectomy mainly in patients with a presumed solitary parathyroid adenoma and missing concordance of preoperative imaging. *Clin Endocrinol (Oxf)* 2007; 66: 878-85.
- Bergenfelz A, Kanngiesser V, Zielke A, Nies C, Rothmund M. Conventional bilateral cervical exploration versus open minimally invasive parathyroidectomy under local anaesthesia for primary hyperparathyroidism. *Br J Surg* 2005; 92: 190-7.
- Fang WL, Tseng LM, Chen JY, Chiou SY, Chou YH, Wu CW, Lee CH. The management of high-risk patients with primary hyperparathyroidism - minimally invasive parathyroidectomy vs. medical treatment. *Clin Endocrinol (Oxf)* 2008; 68: 520-8.
- Greene AK, Mowschenson P, Hodin RA. Is sestamibi-guided parathyroidectomy really cost-effective? *Surgery* 1999; 126: 1036-40.
- Harari A, Zarnegar R, Lee J, Kazam E, Inabnet WB, Fahey TJ. Computed tomography can guide focused exploration in select patients with primary hyperparathyroidism and negative sestamibi scanning. *Surgery* 2008; 144: 970-6.
- Karakayal? FY, Ekici Y, Aliosmano?lu I, Aras M, Genço?lu A, Moray G. Primer hiperparatiroidide ameliyat s?ras?nda ?PTH testi kullan?lmadan yap?lan minimal invaziv paratiroidektomi sonu?lar?m?z. *Ulusal Cerrahi Dergisi* 2008; 24: 27-32.
- Lubitz CC, Stephen AE, Hodin RA, Pandharipande P. Preoperative localization strategies for primary hyperparathyroidism: an economic analysis. *Ann Surg Oncol* 2012; 19: 4202-9.
- Saint Marc O, Cogliandolo A, Pidoto RR, Pozzo A. Prospective evaluation of ultrasonography plus MIBI scintigraphy in selecting patients with primary hyperparathyroidism for unilateral neck exploration under local anaesthesia. *Am J Surg* 2004; 187: 388-93.
- Abdelghani R, Noureldine S, Abbas A, Moroz K, Kandil E. The diagnostic value of parathyroid hormone washout after fine-needle

- aspiration of suspicious cervical lesions in patients with hyperparathyroidism. *Laryngoscope* 2013; 123: 1310-3.
11. Wang TS, Cheung K, Farrokhyar F. Would scan, but which scan? A cost-utility analysis to optimize preoperative imaging for primary hyperparathyroidism. *Surgery* 2011; 150: 1286-94.
 12. Winters R, Friedlander P, Noureldine S, Ekaidi I, Moroz K, Kandil E. Preoperative parathyroid needle localization: a minimally invasive novel technique in reoperative settings. *Minim Invasive Surg* 2011; 2011: 487076.
 13. Zanocco K, Angelos P, Sturgeon C. Cost-effectiveness analysis of parathyroidectomy for asymptomatic primary hyperparathyroidism. *Surgery* 2006; 140: 874-81.
 14. Wong W, Foo FJ, Lau MI, Sarin A, Kiruparan P. Simplified minimally invasive parathyroidectomy: a series of 100 cases and review of the literature. *Ann R Coll Surg Engl* 2011; 93: 290-3.
 15. Solorzano CC, Carneiro-Pla D. Minimizing cost and maximizing success in the preoperative localization strategy for primary hyperparathyroidism. *Surg Clin North Am* 2014; 94: 587-605.
 16. Miccoli P, Barellini L, Monchik JM, Rago R, Berti PF. Randomized clinical trial comparing regional and general anaesthesia in minimally invasive video-assisted parathyroidectomy. *Br J Surg* 2015; 92: 814-8.
 17. Rubello D, Casara D, Saladini G, Piotta A, Pagetta C, Pelizzo MR. 99mTc-MIBI radio-guided surgery in primary hyperparathyroidism: a prospective study of 128 patients. *Tumori* 2005; 88: 63-5.
 18. Kim JP, Park JJ, Son HY, Kim RB, Kim HY, Woo SH. Effectiveness of an i-PTH measurement in predicting post thyroidectomy hypocalcemia: prospective controlled study. *Yonsei Med J* 2013; 54: 637-42.
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