The use of focused, radioguided parathyroidectomy in geriatric patients with a history of thyroid surgery

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Abstract

Objective: Geriatric patients are often reluctant to undergo parathyroid surgery under general anesthesia because of the major comorbidities. The use of minimally invasive techniques for parathyroid lesions under local anesthesia have been published. Radioguided lesion localization has been known to decrease operative time and reduce the occurrence of positive margins in breast cancer surgery. We hypothesize that it could also be effectively used in focused parathyroid surgery in geriatric patients with in history of thyroid surgery. **Materials and Methods:** Our study group consists of geriatric patients with a history of thyroid surgery who underwent focused parathyroid surgery between February 2017 and October 2019. Group-1 included 18 patients who had parathyroidectomy under radioguidance. Group-2, 22 patients who had surgery without it. Patient demographics, operative time, number of frozen sections and length of hospital stay were analyzed. **Results:** Analyzed data were similar between groups. The mean age of the patients was 72.56±12.65 years (range: 65-88). The operative times for group-1 and group-2, were 65.42± 7.78 and 74.63±15.98 minutes, respectively (P=0.002). All patients were discharged uneventfully on postoperative day-2. **Conclusion:** Radioguidance parathyroidectomy positively affected the operative time and also decreased the need for additional frozen section.

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Introduction

Primary hyperparathyroidism (PHPT) is one of the most common endocrine diseases, with a world-wide prevalence near 3% [1, 2]. Due to the increased use of screening programs and biochemical testing, even asymptomatic patients are currently diagnosed at early stages of the disease [3]. Recent studies have shown that median age 55 interval 22-87 years and approximately 2% of all elderly patients have primary hyperparathyroidism [4, 5]. Even though the gold-standard treatment of PHPT is surgery, physicians do not consider surgery as a preferred treatment option for geriatric patients, primarily due to their comorbidities and the elevated risks of general anaesthesia [6]. Nevertheless, it is well known that geriatric patients have symptoms associated with PHPT which can be successfully resolved with surgery [7].

The available literature indicates that 80% of cases of PHPT feature a single-gland adenoma, which may be treated adequately by removal of the diseased gland alone [8]. In 1982, Tibblin et al. (1982) reported the first successful case of unilateral excision of the parathyroid adenoma in patients with single parathyroid adenomas [9]. Moreover, technological advances including high-definition ultrasonography and technetium-99m (^{99m}Tc) sestamibi scintigraphy have enabled the precise identification and localisation of diseased glands and changed surgical algorithms towards more focused operations [10, 11].

Today, minimally invasive parathyroidectomy is recognized worldwide as a surgical technique to treat patients with single-gland PHPT disease [8, 12, 13]. According to reports by the International Association of Endocrine Surgeons, approximately 60% of endocrine surgeons favour the focused parathyroidectomy procedures involving minimally invasive incisions [14]. These minimally invasive techniques include wire-guided localisation (WGL), radioguided localisation (RGL), and video-assisted- or open mini-incisions [15, 16], all of which can also be performed under local anaesthesia [17]. However, as reported by several authors, a major important contraindication for these procedures, is having a history of neck surgery (PNS).

Radioguided localisation was first developed to localize primary, non-palpable breast

lesions and sentinel lymph nodes in breast cancer. This technique has been shown to decrease operative time and reduce the occurrence of positive margins in specimens that are removed during surgery [18]. One of the agents used in RGL, ^{99m}Tc-nanocolloid, is a macromolecule that does not cross over into the blood circulation. In the RGL procedure, ^{99m}Tc-nanocolloid is injected preoperatively into the lesion allowing radiolabeling and subsequent surgical excision of the lesions without any passage into the blood circulation. During surgery, radioactivity is measured by a handheld pencil gamma probe, guiding the surgeon towards the lesion and enabling centering of the excision specimen when it around it. Although the use of gamma radiation might seem hazardous, the radiation doses that are absorbed by the patient and the surgeon are very low, remaining well below the safety limits for radiation and nuclear exposure.

In order to increase the feasibility and the efficacy of minimally invasive parathyroid surgeries, RGL has been applied increasingly, especially in who have in the past received complicated neck surgery. Due to its favourable outcomes, using radioguided surgery for the treatment of solitary parathyroid adenomas has been gaining popularity in recent years [19, 20]. In the present study, our goal was to evaluate the effects of ^{99m}Tc-nanocolloid injections on the outcome of focused parathyroidectomy in geriatric patients with diagnosed primary hyperparathyroidism and a history of thyroid surgery.

Material and Methods

From February 2017 to October 2019, geriatric patients with the history of previous thyroid surgery and underwent focused parathyroid surgery were included to the study. All patients had biochemically verified PHPT disease with preoperative localisation tests including ^{99m}Tc-labelled sestamibi scan imaging and neck ultrasonography for the confirmation of a single-gland disease. Only the patients with concordant results of the sestamibi scan and ultrasonography were included to the study. Focused parathyroidectomy was performed in all patients.

Patients were divided into two study groups according to the use of radiocolloidal guidance and type of anesthesia. Group-1 included patients who underwent surgery under local anesthesia after preoperative ^{99m}Tc-nanocolloid injection for radiocolloidal guidance. Group-2 included patients who underwent focused parathyroid surgery under general anesthesia and without radiocolloidal guidance. The type of anesthesia (local or general) and the use of ^{99m}Tc-nanocolloid were decided based on patient preferences.

Prior to surgery, all adenomas of group-1 patients were injected with 0.1mL of 0.1mCi ^{99m}Tc-nanocolloid to the lesion by a radiologist under ultrasonic guidance.

Surgical technique and anaesthesia

After preoperative administration of intravenous midazolam (0.02mg/kg), a mixture of 1mg/kg 0.25% bupivacaine and 1mg/kg 1% lidocaine were used for local anaesthesia 45 to 120 minutes after injection. Background activity was measured as counts per minute with intraoperative gamma probe, shown in Figure 1, (Navigator standard probe; USSC) placed on the ipsilateral shoulder.

Figure 1. Photo showing Navigator standard probe, USCC.

A 2.5cm transverse incision was performed, under gamma probe guidance. Using gamma-probes, dissection continued while dividing the strap muscles until the site located directly above the localized adenoma was reached. The area of high radioactivity was localized and the count rate was recorded for 10 seconds. The areas with 3 times higher count rate than background was surgically explored and lesions with high radioactivity count were excised. After excision of parathyroid glands, the presence of any remnants of the gland was determined by checking the radioactivity in the cavity. Reduction of the radioactivity level to background levels was taken as a reliable sign of complete removal of the affected gland. As shown in Figure 2, capsule integrity deterioration was not observed macroscopically in any lesion due to radiocolloid injection.

Figure 2. Intraoperative photo of the excised adenoma.

The surgical technique was also almost identical in group-2, the only difference being that the procedure was performed under general anesthesia and radiocolloidal guidance was not used.

A frozen section of the excised specimen and rapid measurement of parathormone levels from blood sample were performed routinely after adenoma removal intraoperatively. The first parathormone measurement was made just after dissection and manipulation of the gland and the second was conducted 10 minutes after removing the gland. Intraoperatively, a PTH level drop ≥50% between the two blood samples was considered indicative of successful gland removal.

All patients were discharged on postoperative day-2 with oral 2gr/day calcium and 1600IU/day vitamin D3 supplementation. Perioperative outcomes including operative time, frozen sections and length of hospital stay were analyzed. Operative time was calculated as skin to skin incision time including the duration of frozen section and quick parathormone analysis.

Statistical analysis

Continuous variables were expressed as mean±standard deviations. Categorical variables were analyzed using the chi-square test or Fisher's exact test, as appropriate. Test results were considered statistically significant if the P-value was less than 0.05.

Results

From February 2017 to October 2019, a total of 89 PHPT patients were underwent focused adenoma surgery in our department. Of these patients, 40 geriatric patients (28 females; 12 males) who also have history of previous thyroid surgery were included to the study. The mean age of these patients was 72.56±12.65 (range: 65-88).

There were 18 patients in group 1 and 22 patients in group 2. The mean preoperative parathormone levels in these groups were 147.72±24.72pg/mL and 142.41±18.03pg/mL, respectively (P=0.357). The mean operative times for group-1 and group-2 were found to be 65.22±9.40 minutes and 74.23±7.81 minutes, respectively (P=0.002). There were four patients in group 2 who required additional analysis of frozen sections because the first specimen contained firm lymph nodes removed as parathyroid adenoma. In group-1, however, no such extra frozen sections were required. In all patients, levels of parathormone and calcium on postoperative day-1 were within the physiological range. No complications such as recurrent laryngeal nerve injury, bleeding or persistent hypoparathyroidism were observed and all patients were discharged uneventfully on postoperative day-2.

Results

As a result of the study, radioguided parathyroidectomy shortens the operation time and reduces the need for frozen section in geriatric population and patients who have previously undergone thyroid surgery. There was no significant difference between the groups in terms of length of hospital stay.

According to Miller et al. (2008), geriatric patients constitute a major subset of patients suffering from primary hyperparathyroidism. They reported that in the NIS database, around 39% of all patients who received parathyroidectomy for primary hyperparathyroidism were aged older than 65 [21]. There are several surgical treatment options for primary hyperthyroidism. Over the last decade, mini-incision focusing procedures (MIP) have become increasingly popular and feasible options in the treatment of primary hyperparathyroidism. Although they were considered contraindicated in the past, MIP can be safely performed on patients with a history of neck surgery [22]. Its advantages include the possibility to perform the procedure under local anaesthesia in outpatient settings, with less tissue dissection, shorter hospital stays, decreased occurrence of hypocalcemia compared to standard bilateral neck explorations, decreased postoperative pain and more aesthetic cosmetic appearance [23-25]. The only disadvantage of these techniques reported is the occurrence of undetected multiglandular disease, or presence of a second adenoma [26, 27]. The benefits of MIP are especially accentuated in geriatric patients who have many possible comorbidities which may put them under higher risk during general endotracheal anaesthesia and bilateral neck exploration. These risks are avoided with MIP as they are performed under local anaesthesia, as an outpatient procedure [28].

The outcomes of MIP have improved with the advent of new preoperative localisation techniques. Pre/intraoperative guidance by ultrasound (USG) and ^{99m}Tc-MIBI single photon emission computed tomography/computed tomography (SPECT/CT) routing are possible tools to identify and locate adenomas. It has been known that USG is user-dependent and when it is performed intraoperatively it may take longer time due to unfamiliar point of view and limited operational area. In addition, SPECT/CT is also a useful technique for preoperative localisation, but it can only give rough anatomical details, which may be misleading in 3 dimension and may look different than surgical view. All these limitations reduce the sensitivity of these techniques [27].

To date, RGL, radioguided seed localization and WGL have been widely used by surgeons mostly for the identification of non-palpable breast tumors [18]. Wire-guided localisation is a commonly accepted and used standard procedure although it has limitations and poses technical challenges that increase cost and morbidity and may necessitate re-operation. Radioguided localisation involves the preoperative injection of a radioactive tracer into the tumor under USG guidance, after which a gamma probe is used intraoperatively to detect the tumor [18]. A systematic review comparing available techniques, showed that the use of RGL produces fewer re-operations, shorter operation times and therefore lower cost than when WGL is used [18].

Despite its proven efficacy in the localisation of tumours during surgery for non-palpable breast cancer, RGL has rarely been tested for the localization of parathyroid glands in pa-

tients undergoing parathyroidectomy. In the literature, Terzioglu et al. (2010) used RGD in thyroid and parathyroid surgery in only 2 of their 21 patients who are mainly suffering from primary hyperparathyroidism [20]. Moreover, their patient group was younger (mean age: 41.5±14.3 years) [20]. Consequently, our study is unique in a way that RGL has never been tested for the localization of parathyroid glands in a geriatric patient group undergoing minimally invasive parathyroidectomy. Accurate localisation is essential in that type of surgery, because the success of MIP critically depend on preoperative localisation of the diseased gland, and concordance with both USG and SPECT imaging [28]. Therefore, any technique that enables and improves localisation will help surgeons to deliver improved, efficient and effective treatment.

Our results show that injection of ^{99m}Tc-nanocolloid into the tumor is an effective technique to localize adenoma that helps to decrease the operative time significantly. This is in line with previous studies in breast cancer patients, which showed that the use of RGL was associated with shorter localization and surgical excision times [29]. We can therefore conclude that the using RGL with ^{99m}Tc-nanocolloid increases the precision and accuracy of tumour localization, thereby increasing the efficacy of MIP.

We observed a similar effect in normal cases even when performing revision surgery. Moreover, although the effect was not statistically significant, in the patient group receiving RGL, a trend could be observed towards decreased numbers of frozen section examinations compared to the number routinely performed in the RGL group.

Limitations of our study include its retrospective design, the relatively small number of patients examined as well as the absence of detailed cost-effectiveness analyses. However, as far as we are aware, there is still scant data regarding the use of RGL with ^{99m}Tc-nanocolloid in subgroups especially as geriatric patients, patients with history of previous neck procedures, and with the combination of local anesthesia.

In conclusion, the results of our study therefore provide new insights in the application of this technique in PHPT patients. However, prospective randomized controlled trials with a higher number of patients are needed to produce robust data confirming and extending the current results.

Bibliography

1. Philippon M, Guerin C, Taieb D et al. Bilateral neck exploration in patients with primary hyperparathyroidism and discordant imaging results: a single-centre study. *Eur J Endocrinol* 2014; 170(5): 719-25.
2. Langdahl B. L, Ralston S. H. Diagnosis and management of primary hyperparathyroidism in Europe. *QJM* 2012; 105(6): 519-25.
3. Kim HG, Kim WY, Woo SU et al. Minimally invasive parathyroidectomy with or without intraoperative parathyroid hormone for primary hyperparathyroidism. *Ann Surg Treat Res* 2015; 89(3): 111-6.
4. Lindstedt G, Nyström E, Lundberg PA et al. Screening of an elderly population in primary care for primary hyperparathyroidism. *Scand J Prim Health Care* 1992; 10(3): 192-7.
5. Makay Ö, Özçınar B, Şimşek T et al. Regional Clinical and Biochemical Differences among Patients with Primary Hyperparathyroidism. *Balkan Med J* 2017; 34(1): 28-34.
6. Chen H, Parkerson S, Udelsman R. Parathyroidectomy in the elderly: do the benefits outweigh the risks? *World J Surg* 1998; 22(6): 531-5; discussion 535-6.
7. Murray SE, Pathak PR, Pontes DS et al. Timing of symptom improvement after parathyroidectomy for primary hyperparathyroidism. *Surgery* 2013; 154(6): 1463-9.
8. Bergenfelz A, Kanngiesser V, Zielke A et al. Conventional bilateral cervical exploration versus open minimally invasive parathyroidectomy under local anaesthesia for primary hyperparathyroidism. *Br J Surg* 2005; 92(2): 190-7.
9. Tibblin S, Bondeson AG, Ljungberg O. Unilateral parathyroidectomy in hyperparathyroidism due to single adenoma. *Ann Surg* 1982; 195(3): 245-52.
10. Küçük NO, Arican P, Koçak S, Aras G. Radioguided surgery in primary hyperparathyroidism. *Ann Nucl Med* 2002; 16(5): 359-62.
11. Özdemir E, Genç M, Aydos U et al. Comparison of ^{99m}Tc-MIBI planar scintigraphy, SPET/CT and ultrasonography in detection of parathyroid adenoma in patients with primary hyperparathyroidism. *Hell J Nucl Med* 2020; 23(1): 21-6.
12. Chow TL, Choi CY, Lam SH. Focused parathyroidectomy without intra-operative parathyroid hormone monitoring for primary hyperparathyroidism: results in a low-volume hospital. *J Laryngol Otol* 2015; 129(8): 788-94.
13. Duh Q.Y. Presidential Address: Minimally invasive endocrine surgery-standard of treatment or hype? *Surgery* 2003; 134(6): 849-57.
14. Rubello D, Casara D, Giannini S et al. Minimally invasive radioguided parathyroidectomy: an attractive therapeutic option for elderly patients with primary hyperparathyroidism. *Nucl Med Commun* 2004; 25(9): 901-8.
15. Denham DW, Norman J. Cost-effectiveness of preoperative sestamibi scan for primary hyperparathyroidism is dependent solely upon the surgeon's choice of operative procedure. *J Am Coll Surg* 1998; 186(3): 293-305.
16. Miccoli P, Bendinelli C, Berti P et al. Video-assisted versus conventional parathyroidectomy in primary hyperparathyroidism: a prospective randomized study. *Surgery* 1999; 126(6): 1117-21; discussion 1121-2.
17. Kelly CW, Eng CY, Quraishi MS. Open mini-incision parathyroidectomy for solitary parathyroid adenoma. *Eur Arch Otorhinolaryngol* 2014; 271(3): 555-60.
18. Lovrics PJ, Cornacchi SD, Vora R et al. Systematic review of radioguided surgery for non-palpable breast cancer. *Eur J Surg Oncol* 201; 37(5): 388-97.
19. Marx S.J. Hyperparathyroid and hypoparathyroid disorders. *N Engl J Med* 2000; 343(25): 1863-75.
20. Terzioğlu T, Senyurek YG, Tunca F et al. Excision efficiency of radioguided occult lesion localization in reoperative thyroid and parathyroid surgery. *Thyroid* 2010; 20(11): 1271-8.
21. Miller BS, Dimick J, Wainess R, Burney RE. Age- and sex-related incidence of surgically treated primary hyperparathyroidism. *World J Surg* 2008; 32(5): 795-9.
22. Spiros D, Nikolaos R, Ioannis C. Minimally invasive parathyroidectomy in patients with previous endocrine surgery. *JSLS* 2011; 15(4): 499-503.
23. Chapuis Y. New directions in the surgical treatment of primary hyperparathyroidism. *Bull Acad Natl Med* 2003; 187(3): 493-502.
24. Haciyanli M, Genc H, Damburaci N et al. Minimally invasive focused parathyroidectomy without using intraoperative parathyroid hormone monitoring or gamma probe. *J Postgrad Med* 2009; 55(4): 242-6.
25. Thakur A, Sebag F, Slotema E et al. Significance of biochemical parameters in differentiating uniglandular from multiglandular disease and limiting use of intraoperative parathormone assay. *World J Surg* 2009; 33(6): 1219-23.
26. Irvin GL 3rd, Carneiro DM. "Limited" parathyroidectomy in geriatric patients. *Ann Surg* 2001; 233(5): 612-6.
27. Kuzminski SJ, Sosa JA, Hoang JK Update in Parathyroid Imaging. *Magn Reson Imaging Clin N Am* 2018; 26(1): 151-66.
28. Teksoz S, Bukey Y, Ozcan M et al. Minimal invasive parathyroidectomy with local anesthesia for well-localized primary hyperpara-

thyroidism: "Cerrahpasa experience". *Updates Surg* 2013; 65(3): 217-23.
29. Sajid MS, Parampalli U, Haider Z, Bonomi R. Comparison of radio-guided occult lesion localization (ROLL) and wire localization for non-palpable breast cancers: a meta-analysis. *J Surg Oncol* 2012; 105(8): 852-8.