International Journal of Surgery 39 (2017) 229–233

Contents lists available at ScienceDirect

International Journal of Surgery

journal homepage: www.journal-surgery.net

Original Research

Feasibility and safety of minimally invasive radioguided parathyroidectomy using very low intraoperative dose of Tc-99m MIBI☆

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HIGHLIGHTS

- Radiotracer dose of 1 mCi presented a very high cure rate.
- Eliminating frozen section analysis did not affect the success rate.
- This protocol (1 mCi) was found to be useful in patients with ectopic glands.

ARTICLE INFO

Article history:
Received 28 October 2016
Received in revised form
23 January 2017
Accepted 8 February 2017
Available online 10 February 2017

Keywords:
Primary hyperparathyroidism
Gamma probe
Minimally invasive parathyroidectomy
Radioguided parathyroidectomy
Radiation exposure
Ectopic parathyroid adenoma

ABSTRACT

Background: Surgical resection of the abnormal parathyroid glands is the only curative treatment for primary hyperparathyroidism (PHPT). Radioguided parathyroidectomy with technetium-99m (TC-99m) sestamibi has been successfully used in patients with PHPT.
This study was designed to evaluate the results of a series of patients with PHPT who underwent minimally invasive radioguided parathyroidectomy (MIRP) using very low dose (1 mCi) of TC-99m sestamibi (MIBI) without application of intraoperative parathyroid hormone (PTH) assay or frozen section analysis.
Methods: Eighty-seven patients with PHPT were prospectively studied from November 2012 to January 2015. Following neck ultrasound (US) and MIBI scan concordant for single gland disease, patients underwent MIRP using a handheld gamma probe. The technique involved injecting of 1 mCi MIBI in the operative room before the beginning of the intervention. All patients were followed up for a minimum of 6 months postoperatively.
Results: MIRP was successfully performed in 86 out of 87 patients (98.85%). The Gamma probe was particularly useful in detection of ectopic parathyroid adenomas in upper mediastinum. Mean operative time was 23.95 ± 7.982 min and mean hospital stay was 1.44 ± 0.604 days. No major surgical complications were recorded.
Conclusions: The MIRP technique using very low dose (1 mCi) of Tc-99m MIBI without intraoperative PTH assay and frozen section analysis resulted in excellent cure rate for PHPT. This technique involves a radiation exposure to patients and surgical staffs 20 times lower than conventional MIRP using 20 mCi Tc-99m MIBI. Besides, patients with PHPT due to ectopic parathyroid adenoma may especially benefit from MIRP.

1. Introduction

Primary hyperparathyroidism (PHPT) is due to excessive secretion of parathyroid hormone (PTH) by one or more enlarged parathyroid glands [1]. Since the introduction of routine serum

☆ This paper has never been presented before.
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http://dx.doi.org/10.1016/j.ijsu.2017.02.009
1743-9191/

calcium measurement in the 1970s, this disorder has become one of the most common endocrine diseases in the world [2]. In Europe and North America, the estimated prevalence of PHPT is between 0.5 and 3 per 1000, although in Asia it seems to be lower, especially in those countries where serum calcium is not yet routinely measured. It is most common among elderly women [3–5].

In general, Single parathyroid adenomas account for PHPT in more than 80% of cases. Less common causes include multiple parathyroid adenoma, parathyroid hyperplasia and parathyroid carcinoma [6].

The first successful surgical resection of parathyroid glands was performed in 1925 with bilateral neck exploration and for many years it remained the standard treatment for PHPT [7,8]. This time-consuming technique, based on identification of all parathyroid glands by using frozen section and excision of any grossly enlarged gland, yields a 95% success rate without significant morbidity [9].

After initial experience with Tc-99m sestamibi (MIBI) for myocardial perfusion studies, it was incidentally observed that this tracer shows significant uptake and retention in the abnormal parathyroid glands of patients with PHPT [10]. Successful utilization of Tc-99m sestamibi (MIBI) imaging for localizing abnormal parathyroid glands was subsequently confirmed by numerous studies and has become the parathyroid imaging technique worldwide [11]. High-quality MIBI parathyroid scintigraphy can accurately localize parathyroid adenomas in 85%–95% of patients with PHPT [12].

With the advent of Tc-99m sestamibi (MIBI) scintigraphy to identify and locate the parathyroid adenoma preoperatively, the era of focused exploration or minimally invasive parathyroidectomy (MIP) began [13]. MIP gradually replaced the traditional bilateral neck exploration as the procedure of choice in many institutions, with comparable cure rates [14]. The different techniques associated with MIP include radioguided exploration and novel endoscopic techniques.

Different MIRP protocols have been studied and now are practiced. Norman and Cheda performed scintigraphy on the day of surgery. Patients were administered a 20 mCi dose of Tc-99m sestamibi in the nuclear medicine department for parathyroid scintigraphy and MIRP was performed 3 h later. This protocol offers the advantage of performing parathyroid scintigraphy and surgery on the same day, though this protocol was basically introduced to rule out ectopic adenoma during conventional bilateral neck exploration [13].

Later, another protocol was introduced by Mariani and Rubello et al. Parathyroid MIBI scan was performed a few days before surgery usually with a double tracer subtraction imaging protocol. A 20 mCi dose of Tc-99m sestamibi was injected in the operating room just before the start of the operation. They also used intraoperative PTH assay and frozen section analysis to make sure that the procedure was successful. It is also known as single-day protocol which possibly improves the chance of identification of parathyroid lesions with rapid Tc-99m sestamibi washout [15].

Use of the gamma probe for measuring ex vivo radioactivity of the removed specimen and surgical field helps in verifying the effective removal of parathyroid tissue and evaluating the success of surgery [16]. The so-called “20% rule” proposed by Murphy and Norman has been reported to yield a 100% accuracy in distinguishing solitary parathyroid adenomas from hyperplasia in patients with PHPT [17].

Other relevant changes in the management of PHPT have been the introduction of intraoperative quick PTH assay. This assay measures serum intact PTH level and can be performed during the operation. Intact PTH has a half-life of 2–3 min. Therefore, a significant drop in PTH level is observed 5–10 min after removal of the abnormal gland. A fall in PTH level $\geq$50% of the preoperative level is considered indicative of successful intervention [18]. It is demonstrated that the sensitivity, specificity and accuracy rate of intraoperative PTH assay are 97%, 100% and 97% respectively [19].

Techniques of using radiolabeled tracers for intraoperative identification of target tissues are critical to MIRP and many other procedures as sentinel node mapping for breast cancer and malignant melanoma, and seed localization during breast lumpectomy [20–23]. Due to concern regarding radiation exposure to the surgical staffs and patients during these procedures, many studies have been conducted to evaluate using lower doses of radioactive tracers for diagnostic and therapeutic purposes.

The purpose of the current study is to evaluate the results of MIRP using very low dose of Tc-99m MIBI (1 mCi) in patients with concordant Ultrasound and MIBI parathyroid scintigraphy for single adenoma. Specifically, we wish to evaluate the results of MIRP alone, without intraoperative PTH assay and frozen section analysis. We also wish to evaluate MIRP using very low dose MIBI in identification and removal of single ectopic mediastinal glands on MIBI parathyroid scintigraphy, therefore this group of patients are not excluded.

2. Methods

The present study is a prospective observational study of eighty-seven patients with PHPT operated on by a single surgeon between November 2012 and January 2015. Clinical manifestations of these patients are presented and all of them underwent cervical ultrasonography and MIBI parathyroid scintigraphy preoperatively. A diagnosis of PHPT was based on hypercalcemia and an elevated serum intact parathyroid hormone level in department of Endocrinology.

All patients with underwent dual-phase imaging consisting of the acquisition of anterior and anterior oblique planar images 15 min after intravenous injection of 20–25 mCi Tc-99m sestamibi. Similar views were acquired 60–150 min postinjection using identical acquisition parameters. Patients who had a MIBI scan interpreted as demonstrating a single focus of pathologically increased activity in the neck (positive) were considered eligible for the MIRP procedure only if Ultrasound findings were concordant with MIBI scans confirming a single adenoma responsible for PHPT. The exclusion criteria included a family history of parathyroid disease, nodular goiter, inflammatory thyroid disease and pregnancy. All patients were discussed completely about the new technique and potential need for second surgery if the procedure failed as a result of using very low dose of MIBI. Informed consent were received from all patients. Patients who did not accept to participate in the study underwent the operation using standard higher dose of MIBI and did not included.

Patients were injected with MIBI, 1 mCi, 15 min before the start of the surgical procedure in the operating room. After induction of the preferred anesthesia (regional or general), external scanning was performed to locate the hot spot by the hand-held gamma probe (Europrobe, GMS, France). A 2–3 cm transverse incision was made in directly over the identified hot spot and was extended for better exposure if necessary. The gamma probe was then inserted into the skin incision and dissection from this point on was guided toward the location with highest radioactivity. Care was taken visualize and preserve the recurrent laryngeal nerve. Once the targeted gland was removed, the radioactivity of the presumed adenoma was measured ex vivo with the probe directed away from the patient and compared to counts obtained by slowly tracking the probe over the background surgical field. If the ex vivo radioactivity totaled at least 20% of the remaining background counts or the ratio between the ex vivo specimen counts and the background counts was greater than 1.2, successful excision of adenoma was