Annals of Medicine and Surgery 7 (2016) 42–47

Contents lists available at ScienceDirect

Annals of Medicine and Surgery

journal homepage: www.annalsjournal.com

# Evaluation of the minimally invasive parathyroidectomy in patients with primary hyperparathyroidism: A retrospective cohort study

Sayoko Toriie [a], Takeki Sugimoto [a], Norihiro Hokimoto [a], Taku Funakoshi [a], Maho Ogawa [a], Toyokazu Oki [a], Ken Dabanaka [a], Tsutomu Namikawa [a,*], Akihiro Sakurai [b], Kazuhiro Hanazaki [a]

[a] Department of Surgery, Kochi Medical School, Kochi University, Japan
[b] Department of Genetic Medicine, Sapporo Medical University, Japan

## HIGHLIGHTS

- We examined diagnostic accuracy for 48 patients with primary hyperparathyroidism.
- All 39 patients in the MIBI-positive group were diagnosed with a single adenoma.
- The preoperative diagnostic accuracy in MIBI-negative patients was only 50%.
- We advise minimally invasive parathyroidectomy is avoided in MIBI-negative patients.

## ARTICLE INFO

*Article history:*
Received 24 November 2015
Received in revised form
4 March 2016
Accepted 4 March 2016

*Keywords:*
Primary hyperparathyroidism (PHPT)
Minimally invasive parathyroidectomy (MIP)
Tc-99m sestamibi scintigraphy
Hypercalcemia

## ABSTRACT

*Introduction:* An accurate differential diagnosis between single adenoma (SA) and multiglandular disease (MGD) remains difficult in Technetium-99m sestamibi scintigraphy (MIBI)-negative patients with primary hyperparathyroidism (PHPT). The aim of the present study was to evaluate the minimally invasive parathyroidectomy (MIP) in patients with PHPT.

*Methods:* Clinical records of 48 patients who underwent neck exploration between November 2002 and June 2012 in Kochi Medical School Hospital were reviewed retrospectively to identify candidates that underwent for MIP which was defined as the selective removal of a SA using less invasive surgery.

*Results:* The preoperative detection rate of lesions using ultrasonography, MIBI, computed tomography, and magnetic resonance imaging was 90%, 83%, 76%, and 55%, respectively. Although all 39 patients in the MIBI-positive group were diagnosed with an SA and subsequently underwent curative MIP, 3 patients in MIBI-negative group ($n = 6$) were MGD, who underwent neck exploration. Preoperative mean intact parathyroid hormone (419 pg/ml vs. 149 pg/ml; $P < 0.01$) and alkaline phosphatase levels (746 U/l vs. 277 U/l; $P < 0.01$) were significantly higher in the SA than MGD group.

*Conclusions:* In MIBI-negative patients with indications for surgery, MIP should not be carried out without a clear localization of SA, or in MGD.



## 1. Introduction

Primary hyperparathyroidism (PHPT) is a generalized disorder of calcium, phosphate, and bone metabolism caused by increased secretion of parathyroid hormone. PHPT is a relatively common disease, with an estimated prevalence of 0.3% of the population [1]. In approximately 80% of PHPT cases, a benign single adenoma (SA) is responsible, whereas multiple adenomas, parathyroid hyperplasia, and parathyroid cancer account for approximately 5%, 15%, and <1% of cases, respectively [2].

Traditionally, symptomatic PHPT presents various symptoms of hypercalcemia, such as fatigue, nausea, dysorexia, peptic ulcer disease, diarrhea, changes in mental status, recurrent kidney stones, and bone discomfort or evidence of bone loss [1].

The traditional gold standard surgical treatment for PHPT is bilateral neck exploration (BNE) to identify all parathyroid glands and remove the adenomas. Based on the assumption that most cases of PHPT are due to an SA, curative excision of the affected

* Corresponding author. Department of Surgery, Kochi Medical School, Kochi University, Kohasu, Oko-cho, Nankoku-City, Kochi, 783-8505, Japan.
*E-mail address:* tsutomun@kochi-u.ac.jp (T. Namikawa).

http://dx.doi.org/10.1016/j.amsu.2016.03.003

gland following unilateral neck exploration (UNE), including identification of the ipsilateral normal parathyroid, was explored in the early 1980s as a new treatment for PHPT. Recently, minimally invasive parathyroidectomy (MIP) with adequate preoperative imaging for the selective removal of a SA has replaced BNE or UNE [3–5]. To improve the cure rate, patients must be carefully selected for MIP to ensure that only SA exists and to exclude multiglandular disease (MGD), including hyperplasia and multiple adenomas. Specifically, MIP is indicated in selected patients with PHPT caused by an SA.

Ogo et al. [6] suggested that surgical indications for asymptomatic PHPT should be determined in general according to the revised guidelines of the Fourth International Workshop on the Management of Asymptomatic PHPT, which provides recommendation for a surgical approach along with monitoring those who do not undergo parathyroid surgery [7]. Surgery is always an option because it is the only definitive therapy for PHPT, while surgery is not mandatory in some patients with asymptomatic disease. In addition, it is desirable that technetium-99m sestamibi (MIBI) scintigraphy be performed whenever possible, because this modality plays an important role in determining whether surgery is appropriate [6]. MIBI has proved to be one of the most reliable modalities for the localization of affected parathyroid glands, including differential diagnoses between SA and MGD. Unfortunately, obtaining an accurate differential diagnosis between SA and MGD in MIBI-negative patients remains difficult. The aim of the present retrospective study was to evaluate the characteristics of patients with PHPT who underwent MIP.

## 2. Patients and methods

The clinical records of 49 consecutive patients who underwent primary parathyroidectomy for PHPT between November 2002 and June 2012 in Kochi Medical Hospital were reviewed retrospectively (Fig. 1). One patient with cancer was excluded, but the remaining 48 patients (44 with SA and four with MGD) were included in the study. Medical records were obtained for all 48 patients, including information regarding the patients' clinical condition, laboratory data for intact parathyroid hormone (iPTH; upper limit of normal (ULN) 65 pg/mL), serum calcium (s-Ca; ULN 10.4 mg/dL), phosphate (ULN 5.3 mg/dL), and alkaline phosphatase (ALP; ULN 340 U/L) and diagnostic imaging for MIBI, ultrasonography (US), computed tomography (CT), or magnetic resonance imaging (MRI). Unfortunately, data regarding creatinine clearance (CCr) and bone mineral density (BMD) are incomplete because these parameters were not measured in all patients in this series.

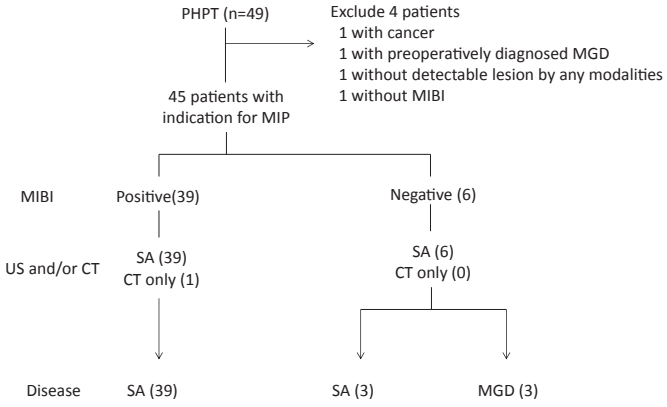


**Fig. 1.** Flowchart showing patient disposition in the present study. PHPT, primary hyperparathyroidism; SA, single adenoma; MGD, multiglandular disease; MIBI, technetium-99m sestamibi scintigraphy; MIP, minimally invasive parathyroidectomy; US, ultrasound; CT, computed tomography.

In Kochi Medical Hospital, MIP is indicated for patients who are diagnosed preoperatively as having an SA. In contrast, BNE is indicated in patients diagnosed preoperatively with MGD. Although defining the term "cure" after surgery is difficult, in the present study we defined a "cure" as restoration of both iPTH and s-Ca levels to within the normal range with no re-elevations for >1 year of follow-up. To perform MIP, mini-cervicotomy on midline or just above the tumor is made according to a precise preoperative localization of the adenoma. After an intraoperative confirmation of tumor, an adequate resection is performed, resulting in less invasive surgical procedure.

This study was fully compliant with the STROBE criteria [8], registering to the Research Registration (Research Registration Unique Identifying Number, researchregistry491). The approval of ethical review board in our institution was waivered according to the Ethical Guideline for Clinical Research issued by Ministry of Health, Welfare and Labor, Japan.

Data are presented as the mean ± SD. The significance of differences was evaluated using unpaired Student's *t*-test. Two-tailed $P < 0.05$ was considered significant.

## 3. Results

### 3.1. Study patients

The present cohort was comprised of 37 women and 11 men, with a mean (range) age of 61 ± 15 (19–87) years. All 48 patients were evaluated preoperatively by US, and MIBI, CT, and MRI were further performed in 47 (98%), 33 (69%), and 11 (23%) patients, respectively. The preoperative detection rate of lesions using US, MIBI, CT, and MRI was 90%, 83%, 76%, and 55%, respectively. In the final diagnosis, 44 patients were found to have an SA and only four had MGD.

Of the 48 patients in the study, 45 (94%) were selected as candidates for MIP (Fig. 1). Three patients were deemed not suitable for MIP: one with a preoperative diagnosis of MGD (final diagnosis MGD), one without detectable PHPT lesions regardless of the imaging modality used (final diagnosis SA), and one who had not undergone preoperative MIBI (final diagnosis SA). The 45 patients who underwent MIP were divided into two groups: an MIBI-positive group (n = 39) and an MIBI-negative group (n = 6). All 39 patients in the MIBI-positive group were diagnosed with an SA and subsequently underwent curative MIP. In the MIBI-negative group, three patients had a final diagnosis of MGD, which would normally exclude MIP. Of these three patients with MGD, two underwent UNE because we suspected MGD on the basis of intraoperative findings. However, one patient was treated with MIP alone because we had no suspicions of MGD during surgery and this patient refused to undergo further radical surgery, such as UNE or BNE, after the initial operation.

### 3.2. Patient characteristics and preoperative findings of patients with an SA and MGD

Preoperative characteristics and symptoms of patients with an SA and MGD are given in Table 1. There were 44 patients (nine men, 35 women) in the SA group and four patients (two men, two women) in the MGD group. The incidence of palpable neck tumor in the SA and MGD groups was 18% and 0%, respectively. Based on their preoperative symptoms, 75%, 11%, and 14% of patients in the SA group were classified as having chemical type, stone type, and bone type PHPT, respectively, compared with 75%, 25%, and 0%, respectively, in the MGD group (see Table 1). None of the patients