Can the use of intraoperative intact-parathyroid hormone monitoring be abandoned in patients with hyperparathyroidism?

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ABSTRACT

BACKGROUND: Ultrasound (US) and technetium-99m sestaMIBI scintigraphy (MIBI) are used to determine the localization of abnormal glands in cases of primary hyperparathyroidism (PHPT). Intraoperative intact-parathyroid hormone (iPTH) monitoring is a reliable examination used to cure PHPT. The aim was to assess the necessity of intraoperative iPTH monitoring.

METHODS: Sixty patients with PHPT were examined using preoperative MIBI and US. The level of iPTH was measured at three time points: 1) at the start of surgery, 2) 10 minutes after gland resection and 3) more than 60 minutes after surgery. We defined a decreased iPTH level as an iPTH level measured 10 minutes after resection that was less than 50% of the preoperative level.

RESULTS: The iPTH levels of 55 patients with concordant lesions decreased to within the normal range more than 60 minutes after surgery. Three of five patients with discordant

images were ultimately cured of PHPT and diagnosed with single parathyroid adenoma.

CONCLUSIONS: It is not necessary to monitor intraoperative iPTH when single concordant lesions are preoperatively identified on both MIBI and US.

INTRODUCTION

There are several diagnostic modalities that can be used as preoperative examinations in patients with primary hyperparathyroidism (PHPT), including ultrasound (US), technetium-99m sesta MIBI scintigraphy (MIBI), magnetic resonance imaging and computed tomography (CT). The use of MIBI for PHPT imaging was first reported in 1989 by Coakley et al. [1]. MIBI is especially useful for determining the preoperative localization of abnormal glands (2-8). US is often used as the first examination for preoperative localization of abnormal glands because it is safe, convenient and inexpensive. Moreover, in the hands of the operating surgeon, US is generally as accurate or more accurate than MIBI (9,10).

In addition to these imaging modalities, intraoperative intact-PTH (iPTH) monitoring is a reliable predictor of successful resection in PHPT patients undergoing parathyroid surgery (11-16). It has also been reported that intraoperative

iPTH monitoring can be used to check the iPTH level as soon as five minutes after extraction of the lesion, thereby ensuring complete resection of the abnormal gland (11). Therefore, intraoperative iPTH monitoring makes minimally invasive surgery possible (17,18). However, not all institutions can perform intraoperative iPTH monitoring due to limitations in the measuring instruments, and many institutions perform surgery on the basis of the preoperative localization determined on both MIBI and US without the use of intraoperative iPTH monitoring.

We conducted this study to examine the necessity of intraoperative iPTH monitoring in PHPT patients. We evaluated whether intraoperative iPTH monitoring is useful for PHPT surgery and whether all PHPT patients should be monitored for intraoperative iPTH. In addition, we also discuss the indications for intraoperative iPTH monitoring in PHPT patients.

METHODS

Sixty-three consecutive patients who underwent parathyroid surgery for PHPT at the Department of Surgery, Nagasaki University Hospital, between January 2003 and July 2010 were enrolled in this study. Three patients were excluded because they had not undergone both MIBI and US to determine their preoperative diagnoses. Therefore, we evaluated a total of 60 patients in this study. The median age of the patients was 58.2 years, and 46 patients were female.

All patients underwent both MIBI and US for preoperative localization of the parathyroid lesions. All resected glands were confirmed to meet the intraoperative histological diagnosis using frozen section examinations. Although there are several criteria for intraoperative iPTH monitoring, the Miami criteria are the most useful. Under these criteria, surgical success is defined by an iPTH drop of 50% or more from the highest of either the preoperative baseline level or the

pre-excision level measured at 10 minutes (12). We measured the iPTH level at three time points: 1) at the start of surgery, 2) 10 minutes after abnormal gland resection and 3) over 60 minutes after surgery. According to the Miami criteria, a complete decrease is defined as an iPTH drop after abnormal gland resection of 50% or more from the highest of either the preoperative baseline level or the pre-excision level measured at 10 minutes. The patients who did not exhibit a decrease in the iPTH level of more than 50% were assigned to the incomplete decrease group.

In cases with concordant imaging lesions on preoperative examination, we performed abnormal gland exploration and completed the surgery. Even if the iPTH level did not decrease, we finished the surgery when the preoperative diagnosis was concordant lesion on MIBI and US.

In cases with two or more abnormal glands or discordant imaging between MIBI and US, we first monitored the

intraoperative iPTH level after performing resection of one of the detected abnormal glands. If the iPTH level was found to have decreased, then we did not look for the other glands. However, if the iPTH level did not decrease, then we searched for the other abnormal glands. The iPTH, calcium and phosphorus levels of all patients were evaluated during long-term follow-up at an outpatient clinic. If the iPTH levels continued to be high, we reexamined the patients with MIBI and US.

RESULTS

Accuracy of preoperative localization

Fifty-six (93.3%) of the 60 patients preoperatively exhibited concordant lesions on MIBI and US. There were four patients (6.7%) with discordant lesions identified on MIBI and US. One patient had a single lesion detected on MIBI and another lesion detected on US, one patient had a single lesion detected on MIBI and double lesions detected on US, one patient exhibited

negative results on MIBI and had double lesions detected on US and one patient had double lesions detected on MIBI and a single lesion detected on US (Table 1).

Intact-PTH Monitoring

Complete decreases were observed in 50 (83.3%) of the 60 patients. Forty-seven (78.3%) of the 50 patients had concordant lesions detected on both MIBI and US at the time of the preoperative diagnosis. Three patients who exhibited complete decreases had discordant lesions detection on MIBI and US. However, the intraoperative iPTH levels of two of these three patients dramatically decreased after resection of one abnormal gland (Table 1). The remaining patient had discordant lesions detected on MIBI and US: two tumors were observed on the preoperative MIBI examination and one tumor was observed on US. After surgery, this patient was suspected to have multiple endocrine neoplasia type I tumors. However, we could not

confirm the diagnosis because the patient dropped out of the follow-up.

Incomplete decrease was observed in 10 patients (16.7%). In nine of these 10 patients, however, the level of iPTH ultimately decreased to within the normal range over 60 minutes after abnormal gland resection. These nine patients had concordant lesions on preoperative MIBI and US. In the remaining patient, the iPTH level was unchanged after one gland resection. Preoperatively, this patient exhibited negative results on MIBI and two lesions on US. Although the intraoperative iPTH level did not decrease after resection of one lesion, it did completely decrease after a second lesion resection. This patient was ultimately diagnosed with double parathyroid adenomas. All 56 patients with concordant results on preoperative MIBI and US indicating the presence of a single lesion were successfully cured by performing an abnormal grand resection (Table 2).

Based on our results, we propose a new PHPT surgical

strategy (Fig. 1). In cases where there are differences in the number of abnormal glands detected on MIBI and US or no uptake is observed on MIBI, intraoperative iPTH monitoring should be performed. In cases with concordant glands detected on MIBI and US, we suggest that intraoperative iPTH monitoring not be used.

DISCUSSION

Although the standard surgery for PHPT involves conventional 4-gland exploration with resection of abnormally enlarged glands, recent advances in preoperative examinations now allow less invasive surgery to be performed. Therefore, making an accurate preoperative diagnosis in patients with PHPT is important for ensuring proper resection of all affected glands. Various methods, including US, CT and MIBI, are currently used for preoperative localization of abnormal glands in patients with PHPT.

US is a safe and easily performed method, and almost all institutions can conduct US examinations. In patients with PHPT, the sensitivity of US is 63-87.5% and the specificity is 90-98.6% (6-8,13,20). A few reports have indicated that surgeon-performed cervical US is more accurate than MIBI (9,10). The use of MIBI for routine diagnosis of PHPT has been gradually increasing. Its sensitivity is generally higher than that of US (3,8,20). The use

of both MIBI and US has improved the accuracy of diagnosis and localization of parathyroid adenomas (13,14,20,21). Brian et al. reported that patients with concordant results between US and MIBI more frequently undergo successful surgery (9). In addition to intraoperative iPTH monitoring, localization of abnormal glands provides a reliable method for ensuring complete resection of the parathyroid glands (11,17,19).

There are several criteria for intraoperative iPTH monitoring. We used the Miami criteria in this study. In our results, the sensitivity was 0.845, the specificity was 0.5, the PPV was 0.980 and the NPV was 0.100 (Table 1). However, for the results of both MIBI and US, the sensitivity was 0.966, the specificity was 1.00, the PPV was 1.00 and the NPV was 0.50 (Table 2). The results of using both MIBI and US might therefore be superior to that of the Miami criteria.

Some reports have indicated that there is a relationship between the use of minimally invasive surgery and intraoperative

iPTH monitoring (6,7,15,16). Jacobson et al. reported that it is not necessary to monitor intraoperative iPTH or use a gamma probe in PTPH patients who undergo preoperative MIBI only. In their study, all patients had single lesions on MIBI and the rate of false negatives was 3% (22). In our study, all patients with concordant lesions on MIBI and US were cured with detected gland resection (true positive 100%). Therefore, the combination of MIBI and US is more accurate at determining the preoperative location of abnormal glands in PHPT patients.

In patients with preoperative discordant lesions on MIBI and US, intraoperative iPTH monitoring should be used, and the possible presence of other parathyroid lesions should be kept in mind. In fact, in our series of patients, we were able to treat double parathyroid adenomas during surgery. In the future, conducting larger prospective studies would be helpful to confirm the present results.

In conclusion, intraoperative iPTH monitoring is very useful in cases presenting with two or more abnormal glands or discordant lesions on MIBI and US. When single concordant lesions are preoperatively identified on MIBI and US examinations, the use of intraoperative iPTH monitoring can be abandoned.

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Fig. 1. The intraoperative iPTH monitoring strategy for PHPT patients. PHPT: primary hyperparathyroidism, MIBI: technetium-99m sestaMIBI scintigraphy, US: ultrasound, iPTH: intact PTH

Table 1
Preoperative diagnosis by MIBI and US

Group	MIBI and US result		total
	Concordant	Discordant	
Complete decrease	47	3	50
Incomplete decrease	9	1*	10
total	56	4	60

MIBI, technetium-99m sesta MIBI scintigraphy
US, ultrasonography
* double adenomas patient

Table 2
Result of treatments of PHPT patients

	Cured **	Not cured***	Total
Concordant	56	0	56
Discordant	2	2*	4
Total	58	2	60

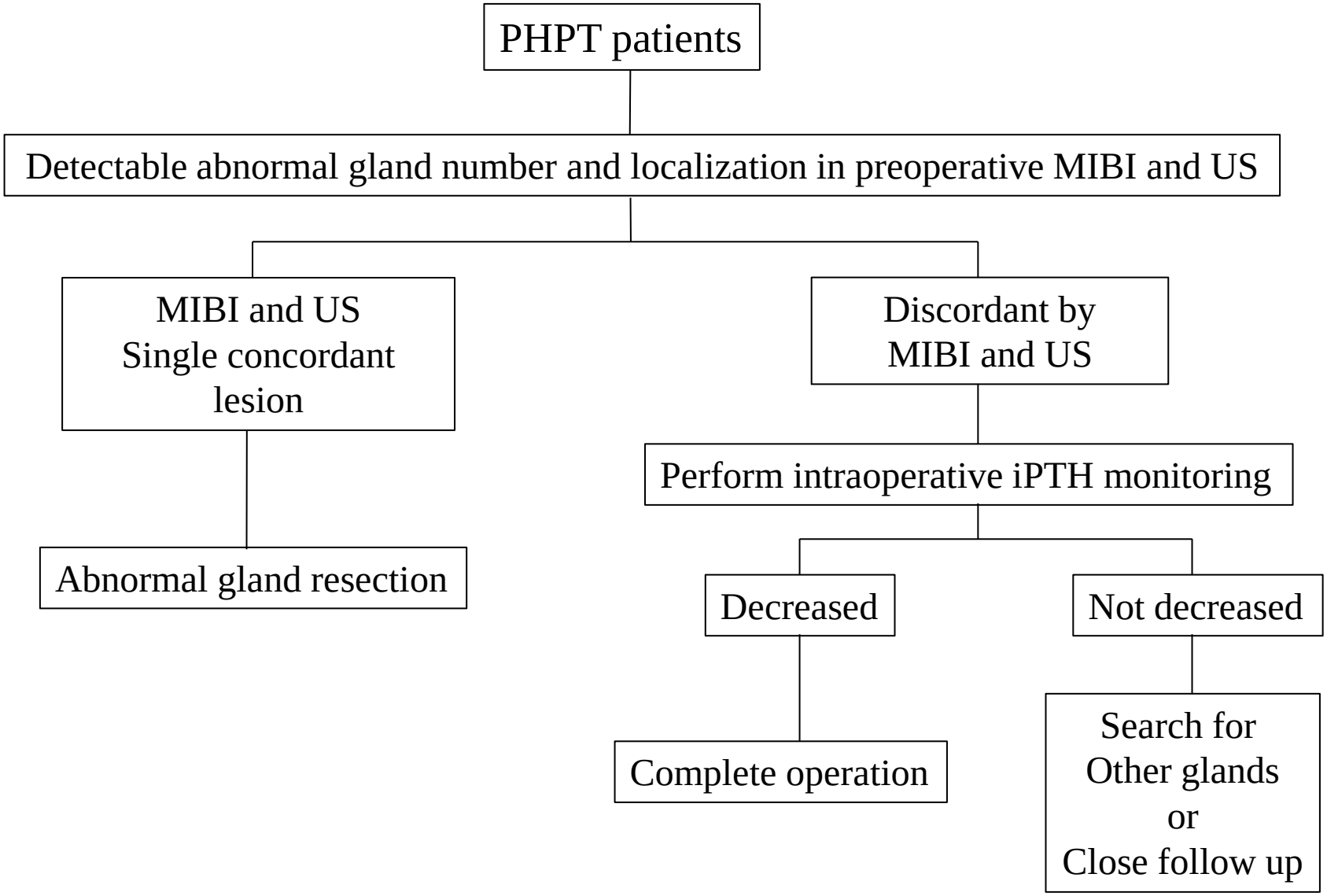
PHPT primary hyperparathyroidism

* MEN type I suspected patient and double adenomas patient

** Cured means postoperative normal iPTH level

*** Not cured means postoperative high iPTH level or resection of an additional gland(s)

Figure 1


PHPT patients
Detectable abnormal gland number and localization in preoperative MIBI and US
MIBI and US
Single concordant
lesion
Discordant by
MIBI and US
Abnormal gland resection
Perform intraoperative iPTH monitoring
Decreased
Not decreased
Complete operation
Search for
Other glands
or
Close follow up