

[ORIGINAL ARTICLE]

Characteristics of Patients with Primary Hyperparathyroidism with Localization Failure of the Causative Parathyroid Gland: A Clinical Report and Literature Review

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Abstract:

Objective It is important to identify the causative parathyroid gland before parathyroidectomy in patients with primary hyperparathyroidism; however, there are some cases of preoperative localization failure. This study assessed the characteristics of patients with failure to localize the causative parathyroid gland.

Methods This study included 114 patients with primary hyperparathyroidism. Physical and biochemical indices were measured, and neck ultrasonography, technetium-99m methoxy isobutyl isonitrile scintigraphy, and magnetic resonance imaging were performed. Localization of the causative gland was confirmed by consensus among multiple physicians.

Results The causative parathyroid glands were localized in 83 patients (73%) with primary hyperparathyroidism. Successful localization was defined as cases in which preoperative imaging accurately identified the causative parathyroid gland, and localization failure included cases with no preoperative identification or those requiring additional resections due to incorrect localization. Most preoperative localization diagnoses in the patients who underwent parathyroidectomy were confirmed to be accurate. Patients with localization failure were significantly older and exhibited lower levels of serum chloride, calcium, intact parathyroid hormone, and urinary calcium values, along with higher serum phosphorus levels, greater phosphate reabsorption, and a smaller tumor size than those with successful localization. Even after adjusting for the age, sex, and body mass index, intact parathyroid hormone levels were significantly associated with successful localization.

Conclusion A relatively old age; low levels of serum chloride, calcium, intact parathyroid hormone, and urinary calcium; high levels of serum phosphorus; phosphate reabsorption; and a relatively small tumor size were associated with localization failure of the causative parathyroid gland.

Key words: primary hyperparathyroidism, parathyroid hormone, chloride, parathyroidectomy

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Introduction

Parathyroid hormone (PTH), produced by the parathyroid glands, plays a key role in regulating calcium (Ca) and phosphorus (P) metabolism. Primary hyperparathyroidism (PHPT) is an endocrine disorder characterized by the autonomous overproduction of PTH by one or more of the four parathyroid glands, leading to hypercalcemia and hypo-

phosphatemia (1, 2). PHPT also contributes to osteoporosis by increasing bone resorption and kidney stones owing to excessive urinary Ca excretion, which may result in an impaired renal function. The prevalence of PHPT is estimated to be 1-2 cases per 1,000 individuals, although this varies depending on screening practices in different countries (1, 3). Therefore, PHPT is considered a common endocrine disorder with significant clinical implications.

The only definitive treatment for PHPT is parathyroidec-

tomy (PTX) (1, 2). PTX has been shown to improve bone mineral density (BMD) (4) and reduce the risk of fractures and kidney stones (5, 6). PTX is recommended not only for patients with symptomatic PHPT but also for those with asymptomatic PHPT, depending on factors such as the serum Ca levels, bone density, renal function, and age (1). Even when these criteria are not strictly met, PTX may still be considered if both the patient and physician agree. Accurate preoperative localization of the causative parathyroid gland is essential for a successful surgery.

Various noninvasive imaging modalities have been employed to identify the causative parathyroid gland, including neck ultrasound (US), single-photon emission computed tomography (SPECT), technetium-99 m (^{99m}Tc) methoxy isobutyl isonitrile (MIBI) scintigraphy, magnetic resonance imaging (MRI), four-dimensional computed tomography (4-D CT), and ^{18}F -choline positron emission tomography/computed tomography (PET/CT) (2). Despite advances in imaging technology, preoperative localization failure still occurs in some cases (1, 7). Although several studies have investigated the effectiveness of different imaging techniques for PHPT, none have comprehensively examined the characteristics of patients who experience localization failure.

The present study therefore investigated the clinical features of PHPT patients with preoperative localization failure of the causative parathyroid gland and summarized these findings in the context of previous reports.

Materials and Methods

This study included 114 patients with PHPT who were admitted to Shimane University Hospital between January 2012 and September 2024. Patients who had previously been treated with calcimimetics such as cinacalcet or evocalcet were excluded. In addition, patients with an estimated glomerular filtration rate (eGFR) of $<30\text{ mL/min/1.73 m}^2$ were also excluded.

This retrospective study was approved by the Ethics Committee of Shimane University Hospital (Approval No. 8,093). As the study used data collected from routine clinical practice, it was disclosed on the hospital's website to allow patients the opportunity to opt out.

Physical indices, including height and weight, were measured, and patients were interviewed regarding their medical history. Blood and urine samples were collected after an overnight fast. The average values of serum Ca and P were calculated from 2 or more measurements. Urinary Ca and P levels were assessed using 24-h urine collection tests, and in most cases, the average of 2 or more measurements was used. PHPT was clinically diagnosed based on inappropriately elevated intact PTH levels in the presence of high-normal or elevated serum Ca levels along with increased urinary Ca excretion. The eGFR was calculated using the equation from the Modification of Diet in Renal Disease Study, which was modified for the Japanese population.

Arterial and venous blood gas analyses were performed.

Hashimoto's thyroiditis was diagnosed when either anti-myeloperoxidase antibody or anti-thyroglobulin antibody was positive. The presence of nephrocalcinosis and urinary stones was determined based on CT findings or a documented past history of these conditions. Patients presenting with subjective symptoms were classified as having symptomatic PHPT.

The BMD was measured at the lumbar spine (LS) 2-4, femoral neck (FN), and distal third of the radius (1/3R) using dual-energy X-ray absorptiometry (QDR-4500 system; Hologic Japan, Tokyo, Japan). T-scores, representing the number of standard deviations from the mean of a young healthy adult population, were used to assess the BMD. Osteoporosis was diagnosed according to the World Health Organization (WHO) criteria: a T-score ≥ -1.0 was considered normal, between -2.5 and -1.0 indicated low bone mass, and ≤ -2.5 indicated osteoporosis (8).

US findings were evaluated by at least two medical professionals. The subcutaneous tissue thickness was defined as the distance from the skin surface to the thyroid isthmus. The maximum tumor diameter was determined using US. The causative parathyroid gland was identified based on typical ultrasonographic features (e.g. visible parathyroid capsule and internal blood flow), high signal intensity on T2-weighted short tau inversion recovery (STIR) MRI, and a radiotracer uptake on ^{99m}Tc MIBI scintigraphy. All imaging results were reviewed at our conferences, and localization of the causative gland was confirmed by consensus among multiple physicians.

All data are presented as mean $\pm$ standard deviation (SD). Statistical significance between groups was assessed using the chi-square test, Fisher's exact test, or unpaired *t*-test, as appropriate. Statistical analyses were performed using the SPSS software program (version 19; International Business Machines, Armonk, USA). Statistical significance was set at $p < 0.05$.

Results

A flow chart of subject enrolment for patients with PHPT is shown (Fig. 1). During the study period, 125 patients with suspected PHPT were admitted to the hospital. Based on clinical interviews and laboratory data, 5 patients were excluded, and 120 patients were clinically diagnosed with PHPT. Among these, six patients were further excluded due to treatment with calcimimetics, severe renal dysfunction, or lack of imaging studies.

The patient characteristics ($n=114$) are shown (Table 1). The majority of participants were elderly women. Normocalcemic PHPT was observed in 21 (18%) patients. None of the patients received vitamin D supplementation prior to the diagnosis. Bone metabolism markers were elevated in the patients, and 82% had osteoporosis. Of those with osteoporosis, 18% received treatment, predominantly bisphosphonates (81%). Few patients had a history of neck surgery, and half of them had nephrocalcinosis or urinary stones.

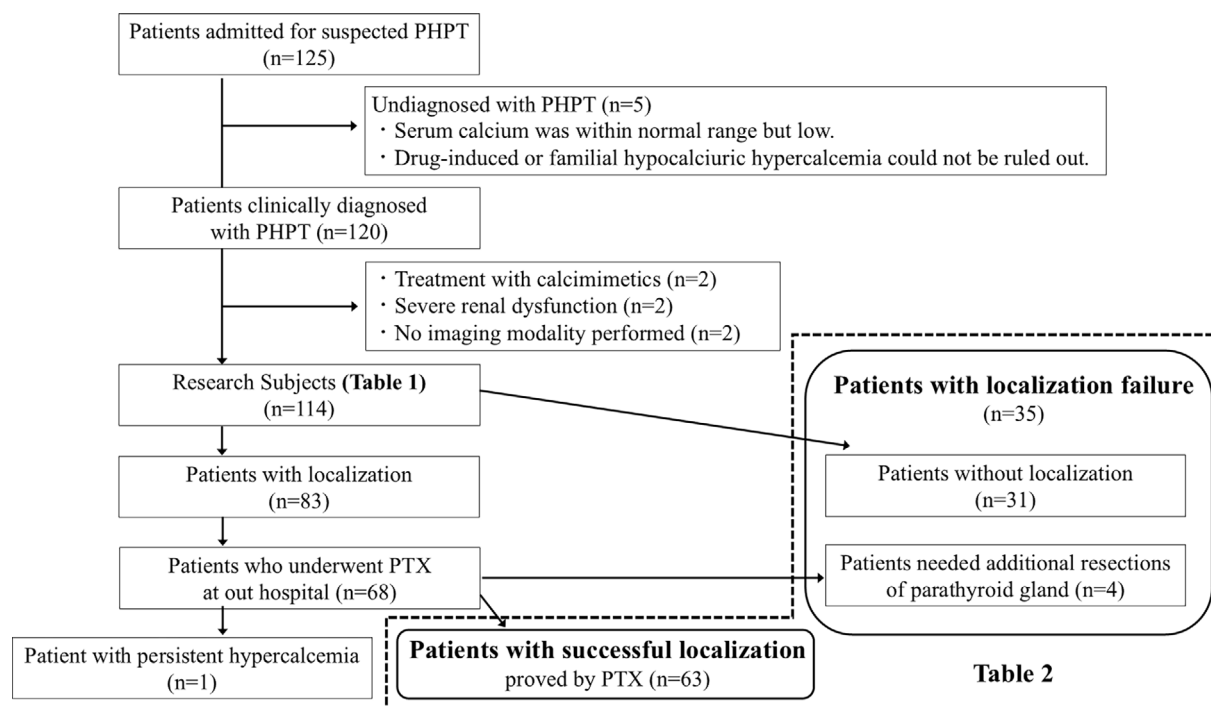


Figure 1. Flow chart of enrolment of patients with primary hyperparathyroidism (PHPT). PTX: parathyroidectomy

Symptomatic PHPT was present in 48% of the cases. One patient was diagnosed with multiple endocrine neoplasia type 1. The causative parathyroid glands were localized in 83 of 114 cases (73%), including 5 cases of ectopic parathyroid glands. All patients underwent neck US and ^{99m}Tc MIBI scintigraphy, with US being the most effective modality for identifying the causative parathyroid gland.

Among the 83 patients with localization, 68 underwent PTX at our hospital and 2 at other hospitals, and 13 declined a surgery. Of the 68 patients who underwent PTX at our hospital, pathological findings revealed adenoma in 66 and hyperplasia in 2. Only one patient with ectopic parathyroid gland did not achieve postoperative calcium normalization. Four patients required additional resections due to an insufficient intraoperative decrease in intact PTH levels despite preoperative localization. Therefore, we defined successful localization as cases in which preoperative localization of the causative parathyroid gland was confirmed to be accurate by postoperative outcomes, as observed in the remaining 63 cases (93%). Conversely, localization failure was defined as cases in which the causative parathyroid gland could not be localized preoperatively (31 cases) or required additional resection owing to inaccurate initial localization (4 cases), totaling 35 cases (Fig. 1).

The characteristics of patients with successful localization and localization failures are shown (Table 2). Patients with localization failure were significantly older ($p<0.05$) and had lower levels of serum chloride (Cl) ($p<0.05$), Ca ($p<0.05$), intact PTH ($p<0.01$), whole PTH ($p<0.01$), and urinary Ca ($p<0.05$), as well as higher levels of serum P ($p<0.05$) and maximal tubular reabsorption of P per GFR (TmP/GFR) ($p<$

0.05), compared to patients with successful localization. In the 78 cases in which the parathyroid gland was identified by neck US, the maximum tumor diameter was measured. Patients with successful localization had significantly larger tumors than those with localization failure (15.1 mm vs. 7.7 mm, $p<0.01$). A correlation analysis showed that intact PTH levels were positively correlated with serum Cl ($r=0.32$, $p<0.01$) and maximum tumor diameter ($r=0.54$, $p<0.01$). Intact PTH was also significantly negatively correlated with hydrogen carbonate (HCO_3^-) ($r=-0.26$, $p<0.05$) but not with potential hydrogen (pH) ($r=0.16$, $p=0.19$). A scatter plot illustrates the relationship between intact PTH and serum Ca levels, comparing patients with successful localization and those with localization failure (Fig. 2).

Three cases were identified using US alone and did not require additional resection. Conversely, three cases identified by other modalities were ectopic adenomas. Among the 63 patients with successful localization, 47 (75%) showed consistent findings across all imaging modalities, while 16 (25%) showed discrepancies. Among the 31 patients without localization, 16 had conflicting results between imaging modalities, and 15 had no identifiable glands on any imaging. These 15 patients had significantly lower intact PTH levels (109 pg/mL vs. 168 pg/mL) and a higher prevalence of Hashimoto's thyroiditis (50% vs. 16%) ($p<0.05$) than those with identifiable glands.

A multivariate logistic regression analysis revealed that intact PTH was significantly associated with successful localization, even after adjusting for the age, sex, and BMI [odds ratio 1.02 (1.01-1.03), $p<0.01$]. The maximum tumor diameter also remained significantly associated after adjust-

Table 1. Baseline Characteristics of Patients with Primary Hyperparathyroidism.

Parameter	
Number of subjects	114
Male (%)	23 (20)
Age (years)	64.3±11.1
Height (cm)	155.2±8.9
Weight (kg)	58.6±12.8
BMI (kg/m ²)	24.2±4.2
Past history of neck surgery (%)	10 (9)
Blood gas analysis (artery 49%), n=75	
pH	7.386±0.028
HCO ₃ ⁻ (mmol/L)	25.0±2.5
U-pH	6.5±0.8
HbA1c (%)	5.8±0.7
Cr (mg/dL)	0.69±0.20
eGFR (mL/min/1.73 m ²)	74.9±20.6
Na (mEq/L)	141±2
K (mEq/L)	4.1±0.4
Cl (mEq/L)	107.5±2.5
Mg (mg/dL), n=112	2.1±0.2
Ca (mg/dL)	10.6±0.7
P (mg/dL)	2.9±0.4
U-Ca (mg/day)	252±114
U-Ca/Cr	0.27±0.12
FECa (%)	1.69±0.64
%TRP (%)	83.6±5.7
TmP/GFR (mg/dL)	2.4±0.5
Intact PTH (pg/mL)	161±126
Whole PTH (pg/mL), n=106	91±58
25(OH) Vitamin D (ng/mL), n=113	15.5±7.5
1,25(OH) ₂ Vitamin D (pg/mL), n=97	91.5±37.3
Free T4 (ng/mL), n=113	1.1±0.2
TSH (μIU/mL), n=113	2.3±1.8
Hashimoto's thyroiditis (%), n=76	15 (20)
BAP (μg/L), n=109	26.1±18.1
Osteocalcin (ng/mL), n=111	32.5±26.9
TRACP-5b (mU/dL), n=108	432±253
U-NTx (nMIBCE/mMCR), n=95	79.1±59.7
LS 2-4 T score, n=108	-2.1±1.4
FN T score, n=111	-2.3±0.9
1/3R T score, n=107	-3.5±1.8
Osteoporosis (%), n=112	92 (82)
Treatment for osteoporosis (%)	21 (18)
Multinodular goiter (%), n=113	72 (64)
Subcutaneous tissue thickness (mm), n=89	4.2±1.9
Isthmus thickness (mm), n=112	2.7±1.4
Nephrocalcinosis or urinary stones (%)	57 (50)
Symptomatic (%)	55 (48)
Identification by	
US (%)	93 (82)
^{99m} Tc MIBI scintigraphy (%)	69 (61)
MRI (%), n=98	72 (74)
Localization (%)	83 (73)
right (%)	42 (51)
left (%)	36 (43)
ectopic (%)	5 (6)
Parathyroidectomy (%)	70 (62)

Values are expressed as means±SD.

BMI: body mass index, pH: potential hydrogen, HCO₃⁻: hydrogen carbonate, HbA1c: hemoglobin A1c, Cr: creatinine, eGFR: estimated glomerular filtration rate, Na: sodium, K: potassium, Cl: chloride, Mg: magnesium, Ca: calcium, P: phosphate, U-Ca: urinary Ca, FECa: fractional excretion of Ca, %TRP: % tubular reabsorption of P, TmP/GFR: maximal tubular reabsorption of phosphorus per GFR, PTH: parathyroid hormone, T4: thyroxine, TSH: thyroid-stimulating hormone, BAP: bone specific alkaline phosphatase, TRACP-5b: tartrate-resistant acid phosphatase 5b, U-NTx: urinary type I collagen cross-linked N-telopeptide, LS: lumbar spine, FN: femoral neck, 1/3R: distal third of the radius, US: ultrasound, ^{99m}Tc: technetium-99m, MIBI: methoxy isobutyl isonitrile, MRI: magnetic resonance imaging

ing for intact PTH level [odds ratio 1.50 (1.16-1.94), *p*<0.05]. In contrast, the statistical significance of other parameters influencing successful localization, such as the serum Cl, Ca, and P levels, urinary Ca excretion, and TmP/GFR, was lost following adjustment for intact PTH.

Discussion

This study identified several clinical and biochemical characteristics associated with failure to localize the causative parathyroid gland in patients with PHPT. Factors such as a relatively old age; low serum levels of Cl, Ca, intact PTH, and whole PTH; reduced urinary Ca excretion; elevated serum P and TmP/GFR values; and a small tumor size were significantly associated with localization failure. In this study, most preoperative localization diagnoses in patients who underwent PTX were accurate, underscoring the importance of precise localization for successful surgical outcomes in PHPT.

However, preoperative localization can be challenging in some cases. Previous studies have shown that normocalcemic PHPT is more difficult to localize than hypercalcemic PHPT, likely because of a higher prevalence of multiglandular disease and smaller adenomas (9). Consistent with these findings, our study also found that lower serum Ca levels are associated with localization failure. In addition, increased levels of intact PTH were associated with successful localization, which is consistent with previous reports (7-11). Autoimmune thyroid diseases (AITD), such as Hashimoto thyroiditis, have also been linked to localization failure (12). In our study, Hashimoto's thyroiditis was significantly associated with failure to identify the suspected parathyroid gland using any imaging modality (*p*<0.05, Table not shown). The characteristic features of AITD, such as coarse thyroid texture and swollen lymph nodes, may interfere with accurate identification via neck US. Although not statistically significant in our study, similar mechanisms may explain the previously reported association between localization failure and multinodular goiter (11-13). The maximum tumor diameter was another significant factor; smaller tumors were more likely to result in localization failure than larger ones, possibly because of limitations in US resolution. An older age, as reported in both our study and previous studies, is also associated with localization failure (7). While some studies have identified high serum creatinine (Cr) levels and lack of experience with US as contributing factors, these were not analyzed or found to be significant in our study (7, 13). In addition, in the present study, low levels of serum Cl and urinary Ca and high levels of serum P and TmP/GFR were associated with localization failure. To summarize the present study and previous reports, low levels of serum Cl, Ca, intact PTH, and whole PTH; reduced urinary Ca; elevated levels of serum P and Cr; increased urinary P reabsorption; small tumors; lack of experience of US operators; older age; hyperplasia; and the presence of AITD or multinodular goiter are thought to be associated with local-

Table 2. Comparison of Parameters between Primary Hyperparathyroidism Patients with Successful Localization and Localization Failure of the Causative Parathyroid Gland.

Parameter	Successful Localization	Localization Failure	P
Number of subjects	63	35	
Male (%)	14 (22)	7 (23)	0.80
Age (years)	62.1±11.4	66.4±8.7	<0.05
Height (cm)	155.6±8.9	155.3±9.5	0.84
Weight (kg)	59.6±13.5	58.0±11.8	0.58
BMI (kg/m ²)	24.5±4.6	24.0±3.9	0.70
Blood gas analysis, n=44/21			
pH	7.392±0.027	7.377±0.029	0.08
HCO ₃ ⁻ (mmol/L)	24.8±2.3	25.2±2.8	0.58
U-pH	6.5±0.8	6.4±0.8	0.82
Cr (mg/dL)	0.67±0.17	0.70±0.18	0.55
eGFR (mL/min/1.73 m ²)	78.1±21.4	72.7±17.7	0.36
Na (mEq/L)	141±2	141±2	0.82
K (mEq/L)	4.1±0.4	4.2±0.4	0.59
Cl (mEq/L)	108.0±2.1	106.6±2.5	<0.05
Mg (mg/dL), n=62/34	2.1±0.2	2.0±0.2	0.16
Ca (mg/dL)	10.7±0.8	10.4±0.6	<0.05
P (mg/dL)	2.8±0.5	3.0±0.3	<0.05
U-Ca (mg/day)	280±113	233±103	<0.05
U-Ca/Cr	0.29±0.11	0.26±0.12	0.09
FECa (%)	1.82±0.68	1.61±0.56	0.12
%TRP (%)	82.6±6.8	84.6±4.1	0.25
TmP/GFR (mg/dL)	2.3±0.5	2.5±0.3	<0.05
Intact PTH (pg/mL)	193±156	110±43	<0.01
Whole PTH (pg/mL), n=58/33	106±69	69±30	<0.01
25(OH) Vitamin D (ng/mL), n=62/35	15.3±8.4	15.6±6.1	0.43
1,25(OH) ₂ Vitamin D (pg/mL) n=57/26	90.5±30.9	97.0±49.4	0.85
Free T4 (ng/mL), n=62/35	1.1±0.2	1.1±0.2	0.29
TSH (μIU/mL), n=62/35	2.3±1.8	2.2±1.8	0.35
Hashimoto's thyroiditis (%), n=43/20	6 (14)	7 (35)	0.06
BAP (μg/L), n=59/34	29.1±19.4	22.6±13.8	0.09
Osteocalcin (ng/mL), n=60/35	38.0±32.7	26.8±15.7	0.09
TRACP-5b (mU/dL), n=57/35	471±283	368±189	0.08
U-NTx (nMIBCE/mMCR), n=53/28	87.7±67.7	68.5±45.2	0.42
LS 2-4 T score, n=60/33	-2.2±1.5	-2.0±1.2	0.57
FN T score, n=62/34	-2.3±0.9	-2.2±0.8	0.52
1/3R T score, n=59/33	-3.3±1.8	-3.8±1.4	0.28
Osteoporosis (%), n=63/34	51 (81)	28 (83)	0.87
Multinodular goiter (%), n=62/35	38 (62)	21 (60)	0.90
Subcutaneous tissue thickness (mm) n=48/31	4.4±2.1	4.0±1.5	0.78
Isthmus thickness (mm), n=62/35	2.8±1.6	2.5±1.2	0.42
Nephrocalcinosis or urinary stones (%)	30 (48)	20 (57)	0.37
Symptomatic (%)	36 (57)	15 (43)	0.18
Identification by			
US (%)	61 (97)	17 (49)	<0.01
Maximum tumor diameter (mm) n=61/16	15.1±7.9	7.7±2.2	<0.01
^{99m} Tc MIBI scintigraphy (%)	50 (79)	6 (17)	<0.01
MRI (%), n=54/34	50 (93)	14 (42)	<0.01

BMI: body mass index, pH: potential hydrogen, HCO₃⁻: hydrogen carbonate, HbA1c: hemoglobin A1c, Cr: creatinine, eGFR: estimated glomerular filtration rate, Na: sodium, K: potassium, Cl: chloride, Mg: magnesium, Ca: calcium, P: phosphate, U-Ca: urinary Ca, FECa: fractional excretion of Ca, %TRP: % tubular reabsorption of P, TmP/GFR: maximal tubular reabsorption of phosphorus per GFR, PTH: parathyroid hormone, T4: thyroxine, TSH: thyroid-stimulating hormone, BAP: bone specific alkaline phosphatase, TRACP-5b: tartrate-resistant acid phosphatase 5b, U-NTx: urinary type I collagen cross-linked N-telopeptide, LS: lumbar spine, FN: femoral neck, 1/3R: distal third of the radius, US: ultrasound, ^{99m}Tc: technetium-99m, MIBI: methoxy isobutyl isonitrile, MRI: magnetic resonance imaging

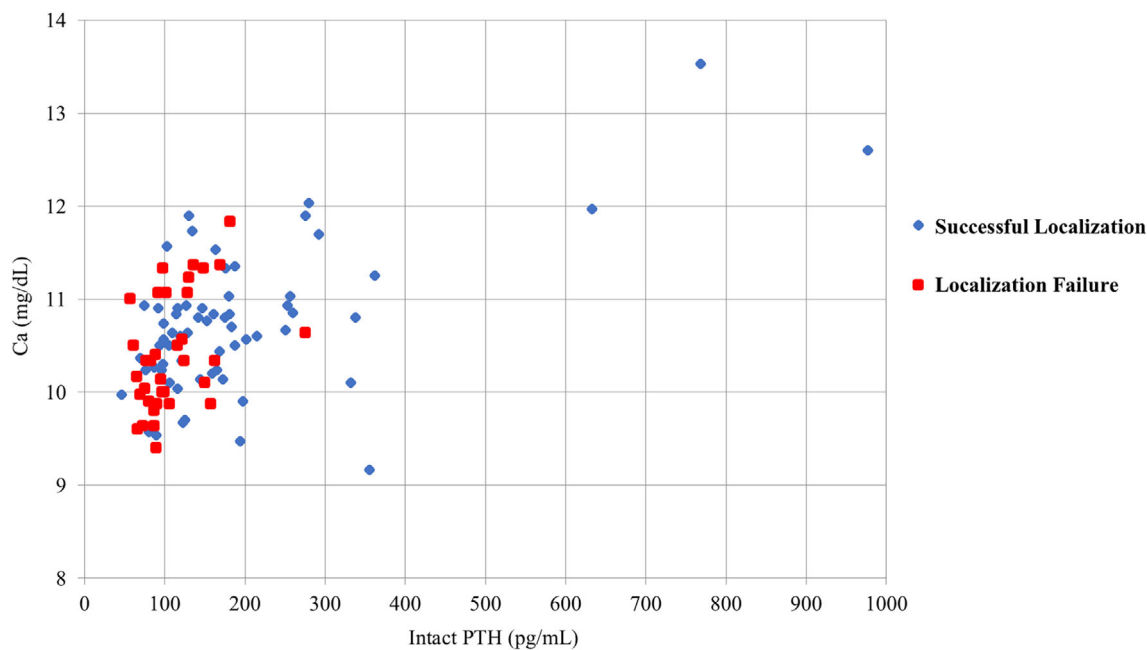


Figure 2. Scatter plot showing the relationship between intact parathyroid hormone (PTH) and calcium (Ca) levels. Blue plot: successful localization, red plot: localization failure.

Table 3. The Characteristics of Primary Hyperparathyroidism Cases with Localization Failure of the Causative Parathyroid Gland.

Patient-related factors	
- Older age	- Laboratory data
- Thyroid diseases	Low levels of chloride
AITD	Low levels of Ca
Multinodular goiter	Low levels of intact PTH
- Parathyroid gland	Low levels of whole PTH
Small tumor	High levels of P
Hyperplasia	High levels of creatinine
	Decreased urinary Ca excretion
	Increased urinary P reabsorption
Provider-related factors	
- Lack of experience	

AITD: autoimmune thyroid diseases, Ca: calcium, PTH: parathyroid hormone, P: phosphate

ization failure (Table 3).

Regarding imaging modalities, previous studies have shown varying effectiveness, depending on the patient’s background and localization criteria. Kowalski et al. have summarized imaging modalities based on Madkhali et al.’s report (Table 4) (2, 14). In addition, combining multiple imaging modalities can increase the sensitivity and specificity (14). Neck US and ^{99m}Tc MIBI scintigraphy are cost-effective first-line screening tools. However, advanced modalities, such as combined SPECT and 4-D CT (4-D SPECT/CT) and ¹⁸F-choline PET/CT have demonstrated greater localization success rates than conventional imaging modalities, albeit with increased cost and radiation exposure (15, 16). This may be particularly useful in cases where

the initial screening fails.

Interestingly, our study found a novel association between low serum Cl levels and localization failure. To our knowledge, this has not been previously reported. In PHPT, decreased HCO₃⁻ reabsorption and increased Cl reabsorption in the proximal tubule can lead to mild hyperchloremic acidosis (17, 18). Liu et al. reported that symptomatic patients with PHPT had higher levels of both PTH and Cl than asymptomatic patients (19). In our study, intact PTH was positively correlated with serum Cl and negatively correlated with HCO₃⁻. This association is supported by the partial correlation analysis and suggests that fluctuations in PTH levels may influence serum Cl and HCO₃⁻, which can affect localization outcomes. Although the mechanistic link remains speculative, further investigation is required.

Several limitations associated with the present study warrant mention. First, the small sample size and single-center design (Shimane University Hospital) may have limited the generalizability of the findings. As a tertiary-care center, our hospital may have a higher proportion of patients with severe diseases than other facilities. Second, the imaging evaluations were based on medical records rather than standardized radiological reviews, introducing potential variability. Third, not all biochemical parameters were consistently measured in all patients. In particular, blood gas analyses included both arterial and venous samples, which may have affected their accuracy. Finally, this study included normocalcemic PHPT in 18% of cases. The possibility of secondary hyperparathyroidism cannot be completely ruled out in patients with concurrent vitamin D deficiency. Further large-scale studies are required in the future.

In conclusion, a relatively old age; low levels of serum Cl, Ca, intact PTH, and whole PTH; reduced urinary Ca lev-

Table 4. The Characteristics of Imaging Modalities.

Imaging	Sensitivity (%)	Specificity (%)	Main advantages	Main disadvantages
Ultrasound	70-80	80-89	-Quick -Cheap -No radiation -Available during surgery	-Low sensitivity for small glands -Low sensitivity for ectopic adenomas
^{99m} Tc MIBI scintigraphy	80-90	78-98	-Minimal radiation	-Limited sensitivity for multiple glands -Long examination time -Difficulty of distinguishing thyroid or parathyroid tumors
MRI	70-80	90-95	-No radiation	-Long examination time -High cost -No available for patients with maintenance of metal objects inside the organism or claustrophobia
4-D CT scan	60-80	85-98	-High sensitivity for smaller glands	-Exposure to radiation -Involves risk of application due to contrast agent -Difficulty of distinguishing parathyroid gland or lymph node

^{99m}Tc: technetium-99m, MIBI: methoxy isobutyl isonitrile, MRI: magnetic resonance imaging, 4-D CT: four-dimensional computed tomography

els; elevated serum P and TmP/GFR values; and a small tumor size were significantly associated with localization failure. Even after adjusting for the age, sex, and BMI, intact PTH levels remained significantly associated with successful localization. Furthermore, the maximum tumor diameter showed a significant association after adjustment for intact PTH levels. This study highlights the importance of evaluating the likelihood of localization failure prior to imaging, which may help guide diagnostic and therapeutic strategies in the early stages of PHPT.

The authors state that they have no Conflict of Interest (COI).

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