


ORIGINAL RESEARCH

Non-adherence to consensus guidelines on preoperative imaging in surgery for primary hyperparathyroidism

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Abstract

Objective: The aim of this study was to determine the adherence to consensus guidelines on preoperative imaging of patients with primary hyperparathyroidism (pHPT) in real local practice.

Methods: This was a retrospective multicenter cohort study of 411 patients undergoing parathyroidectomy for pHPT from 2007 to 2017 in three referral centers.

Results: In 286/411 patients (69%) the preoperative imaging workup adhered to guidelines (utilizing ultrasound and parathyroid scintigraphy). In patients in whom guidelines were followed 63% were discharged within one day versus 37% in whom guidelines were not followed ($P < .0005$). The use of a bimodality imaging workup, starting with ultrasound and parathyroid scintigraphy followed by imaging upscaling aiming for anatomical and functional concordance, was a predictor for the performance of a minimally invasive parathyroidectomy (OR 4.098, 95% CI 2.296-7.315, $P < .0005$).

Conclusion: The level of compliance to preoperative imaging guidelines is suboptimal in this population. Patients in whom adherence was achieved showed a shorter length of stay. More education of physicians is required regarding the appropriate preoperative imaging workup in pHPT.

Level of evidence: 2b (individual cohort study).

KEYWORDS

adherence, endocrine surgery, guideline, preoperative imaging, primary hyperparathyroidism

Abbreviations: AAES, American Association of Endocrine Surgeons; BNE, bilateral neck exploration; CT, computed tomography; cUS, cervical ultrasonography; DXA, dual-energy X-ray absorptiometry; ESES, European Society of Endocrine Surgeons; FHH, familial hypocalciuric hypercalcemia; ioPTH, intraoperative-PTH; MIP, minimal invasive parathyroidectomy; OR, odds ratio; PET, positron emission tomography; pHPT, primary hyperparathyroidism; PS, parathyroid scintigraphy; PTH, parathyroid hormone; SPECT, single-photon emission computed tomography; 25(OH)D, 25-hydroxyvitamin D.

1 | INTRODUCTION

Primary hyperparathyroidism (pHPT) is the predominant cause of hypercalcemia with increasing incidence with advancing age.¹ It is characterized by hypercalcemia due to high concentrations of

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parathormone (PTH), which may lead to symptoms classically known as disease of bones, renal stones, abdominal groans, and psychic moans. The leading cause of pHPT is a solitary adenoma (89%) followed by multiple gland hyperplasia (6%), double adenomas (4%) and parathyroid carcinomas (<1%).²

The only curative treatment for pHPT is surgery. Due to the high occurrence of solitary adenomas, surgery is preferably performed through a minimally invasive parathyroidectomy (MIP). To perform a MIP targeted and accurate, preoperative imaging with a positive result is essential. There is a wide variety of scanning techniques, but there are two main imaging strategies: functional (ie, nuclear) and anatomical/localizing (ie, radiologic).

Because of an increasing availability worldwide, a wide range of imaging modalities are used, leading to high costs and potential heterogeneity in surgical outcomes, even if the success rate is stable. Therefore, the first guideline for the surgical management of pHPT was published by the American Association of Endocrine Surgeons (AAES) in 2016.³ The AAES recommends the combined use of cervical ultrasonography (cUS) (anatomical imaging) and parathyroid scintigraphy (PS) (functional imaging) as first steps in preoperative imaging. This combination of scans has proven to be the most cost-effective strategy,³ is widely available and was also advised by the positional statement of the European Society of Endocrine Surgeons (ESES) in 2009.⁴

The adherence to consensus guidelines on the decision for parathyroidectomy in patients with pHPT in real-practice has been studied by Kuo et al and Yeh et al in two hospitals in the United States.^{5,6} Both studies showed low adherence to guidelines (40%-50%),

emphasizing that non-adherence may be a global problem. Yet, the level of compliance with guidelines on the preoperative imaging workup of patients with pHPT in real-practice is unknown. Here, we show to what extent consensus guidelines for preoperative imaging in patients with pHPT are followed in real practice, and the difference in surgical approach, duration of surgery, and duration of hospitalization between these two groups (ie, adherence vs no adherence to guidelines).

2 | METHODS

2.1 | Study design and patients

This is a multicenter retrospective cohort study of patients with biochemically proven pHPT who underwent a parathyroidectomy in three random hospitals (one university hospital and two general training hospitals) between 2007 and 2017. Patients eligible for inclusion were ≥ 18 years old, diagnosed with biochemically confirmed pHPT, and had undergone parathyroidectomy. Patients were excluded if they were known to have a germline mutation predisposing for multiple gland disease or familial hypocalciuric hypercalcemia (FHH), if an alternative diagnosis (eg, [para]thyroid carcinoma) was known before surgery or if they used lithium in the past or present (Figure 1). From January 2007 to December 2017, a total of 456 patients underwent a parathyroidectomy for pHPT. In addition to the patients who met the exclusion criteria, three pregnant patients were excluded because they could not undergo functional imaging scans, 11 patients were

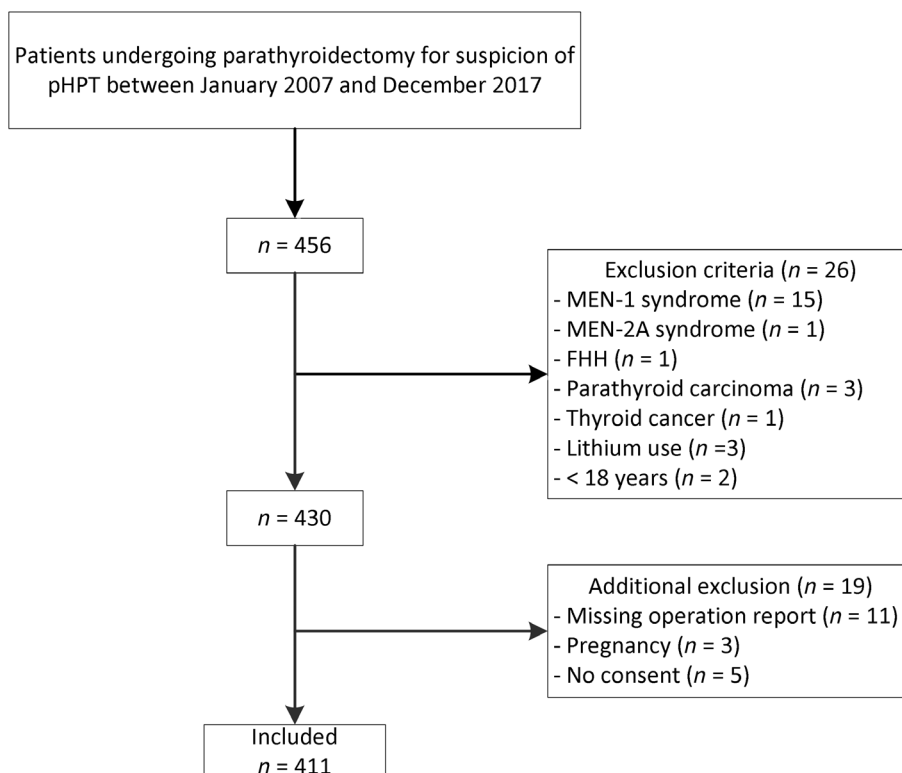


FIGURE 1 Flowchart of patient inclusion. Abbreviations: pHPT, primary hyperparathyroidism; MEN-1, multiple endocrine neoplasia type 1; MEN-2A, multiple endocrine neoplasia type 2A; FHH, familial hypocalciuric hypercalcemia

excluded because the surgical report was missing, and five patients did not give consent. In total, 411 patients met the inclusion criteria (Figure 1). Data from 21 patients were previously published.⁷

The medical charts were reviewed to determine the gender, age, BMI, preoperative blood levels and imaging techniques, surgical and pathology findings, and postoperative blood levels. Corrected calcium was calculated using an online calculator.⁸ The diagnosis pHPT was made based on elevated calcium levels in the setting of inappropriately high-normal or elevated PTH levels.

Data obtained from patient records were anonymously stored using study-specific patient codes in a password-protected database. This study was approved by the Institutional Review Board of all three centers and was exempt for collection of informed consent in two centers, while in one center informed consent was obtained.

2.2 | Preoperative imaging

All patients underwent at least one type of preoperative imaging before parathyroidectomy. Five different imaging modalities were performed: cUS, PS (with or without single-photon emission computed tomography/computed tomography [SPECT/CT]), CT or four-dimensional CT (4D-CT, CT scan during two or more contrast enhancement phases), ¹¹C-methionine PET(/CT) and ¹⁸F/¹¹C-choline PET(/CT).

Adherence to consensus guidelines on preoperative imaging was defined as the utilization of at least cUS and PS.

In addition, two groups were identified: one group in whom a bimodality imaging workup aiming for positive anatomical and functional concordance was performed according to guidelines, and one

group that underwent a rather random imaging workup or did not have cUS and PS as first-line scans. Patients met inclusion criteria for the bimodality group if prior to parathyroidectomy patients underwent an anatomical and functional imaging workup, meaning (a) positive cUS and positive PS that were concordant as suggested by the guidelines or (b) all other cases (positive but discordant cUS and PS, negative cUS and positive PS, positive cUS and negative PS) in whom additional functional or anatomical scans ultimately yielded at least one concordant positive result between one anatomical and one functional imaging modality or (c) patients in whom full upscaling was performed with or without a positive concordant result.^{3,4} All remaining patients with various types of imaging or no initial cUS and PS as first-line scans were assigned to the random imaging group. A low dose CT without intravenous contrast enhancement performed during SPECT/CT or PET/CT was not considered as a separate/diagnostic CT scan.

2.3 | Surgery and pathology

A surgical procedure was classified as a MIP when the surgeon explored on one side of the neck only, either laterally at the medial edge of the sternocleidomastoid muscle or centrally, depending on the surgeon's preference. All MIPs were openly performed. When all four parathyroid glands were exposed or both sides of the thyroid midline were inspected, the operation was classified as a bilateral neck exploration (BNE). The duration of surgery was classified as the time from incision to the time of closure (in minutes, min). The pathology report was reviewed for the final diagnosis. In addition, the gland weight (milligrams, mg) and the largest diameter (millimeters, mm) were recorded.

TABLE 1 Patients' baseline characteristics

Characteristics	Criterion adherence (n = 285)	Criterion no adherence (n = 126)	Total (n = 411)	P value
Gender, No. (%)	65 (23%)	31 (25%)	96 (23%)	.692
Male	(n = 285)	(n = 126)	(n = 411)	
Age (years)	62 ± 13	59 ± 13	61 ± 13	.075
Mean ± SD	(n = 285)	(n = 126)	(n = 411)	
Body mass index (kg/m ²)	27.3 ± 4.5	27.1 ± 4.5	27.2 ± 4.5	.659
Mean ± SD	(n = 215)	(n = 94)	(n = 309)	
Preoperative total serum calcium (mmol/L)	2.89 ± 0.22	2.86 ± 0.21	2.88 ± 0.22	.182
Mean ± SD	(n = 284)	(n = 125)	(n = 409)	
Preoperative albumin-corrected calcium (mmol/L)	2.83 ± 0.24	2.80 ± 0.24	2.82 ± 0.24	.188
Mean ± SD	(n = 252)	(n = 118)	(n = 370)	
Preoperative PTH (pmol/L)	23.4 ± 21.3	27.7 ± 44.2	24.7 ± 30.1	.304
Mean ± SD	(n = 280)	(n = 122)	(n = 402)	
Preoperative creatinine (μmol/L)	84.05 ± 30.35	86.13 ± 32.93	84.68 ± 31.12	.549
Mean ± SD	(n = 269)	(n = 116)	(n = 385)	
Preoperative 25-hydroxyvitamin (nmol/L)	54.92 ± 28.43	56.98 ± 25.06	55.32 ± 27.73	.745
Mean ± SD	(n = 101)	(n = 24)	(n = 125)	

Note: Criterion adherence = utilization of at least cervical ultrasonography and parathyroid scintigraphy. Abbreviation: PTH, parathyroid hormone.

If intraoperative-PTH (ioPTH) was used, it was measured at T0 (before incision), T1 (5 min after excision of the adenoma), T2 (10 min after excision) (and if available T3 [15 min after excision], and T4 [20 min after excision]). A decrease in the ioPTH of at least 50 was classified as a sufficient decrease. Cure was defined as normal serum level calcium (<2.65 mmol/L) at least six months after surgery, and if available normal serum level PTH (2-7 pmol/L).⁹ Persistent HPT was defined as failure to achieve normocalcemia within six months of parathyroidectomy and recurrent HPT as recurrence of hypercalcemia after a normocalcemic interval of more than six months after parathyroidectomy.³

2.4 | Statistics

Categorical variables are displayed as count (n) and percentage (%) and were assessed with chi-square. Continuous variables are displayed by mean \pm SD and were assessed with independent Student's t test.

Patients in whom adherence to guidelines was achieved were compared to patients in whom adherence was not achieved. Univariate logistic regression was performed to identify possible predictors for performing a MIP. In addition, the possible predictors were taken into a multiple logistic regression with backward Wald elimination (removal of variable if P value > .157).¹⁰ Predictors are displayed by the odds ratio

TABLE 2 Preoperative imaging workup

Number and combinations of imaging modalities	Criterion adherence, No. (%)	Criterion no adherence, No. (%)	Total, No. (%)
1. Imaging modality			
PS	0	73 (57.9%)	73 (17.8%)
cUS	0	5 (4.0%)	5 (1.2%)
¹⁸ F-choline PET	0	1 (0.8%)	1 (0.2%)
2. Imaging modalities			
cUS + PS	212 (74.4%)	0	212 (51.6%)
PS + CT	0	20 (15.9%)	20 (4.9%)
PS + ¹¹ C-methionine PET	0	9 (7.1%)	9 (2.2%)
cUS + ¹⁸ F-choline PET	0	4 (3.2%)	4 (1.0%)
PS + ¹⁸ F-choline PET	0	2 (1.6%)	2 (0.5%)
cUS + CT	0	1 (0.8%)	1 (0.2%)
PS + ¹¹ C-choline PET	0	1 (0.8%)	1 (0.2%)
3. Imaging modalities			
cUS + PS + CT	17 (6.0%)	0	17 (4.1%)
cUS + PS + ¹⁸ F-choline PET	13 (4.6%)	0	13 (3.2%)
cUS + PS + ¹¹ C-methionine PET	11 (3.9%)	0	11 (2.7%)
cUS + PS + ¹¹ C-choline PET	7 (2.5%)	0	7 (1.7%)
PS + CT + ¹¹ C-methionine PET	0	7 (5.6%)	7 (1.7%)
cUS + PS + 4D-CT	4 (1.4%)	0	4 (1.0%)
cUS + 4D-CT + ¹⁸ F-choline PET	0	1 (0.8%)	1 (0.2%)
PS + CT + ¹¹ C-choline PET	0	1 (0.8%)	1 (0.2%)
4. Imaging modalities			
cUS + PS + CT + ¹¹ C-methionine PET	11 (3.9%)	0	11 (2.7%)
cUS + PS + 4D-CT + ¹⁸ F-choline PET	3 (1.1%)	0	3 (0.7%)
cUS + PS + ¹¹ C-methionine PET + ¹¹ C-choline PET	3 (1.1%)	0	3 (0.7%)
cUS + PS + CT + ¹¹ C-choline PET	1 (0.4%)	0	1 (0.2%)
PS + CT + ¹¹ C-methionine PET + ¹¹ C-choline PET		1 (0.8%)	1 (0.2%)
cUS + PS + CT + ¹⁸ F-choline PET	1 (0.4%)	0	1 (0.2%)
cUS + PS + 4D-CT + ¹¹ C-choline PET	1 (0.4%)	0	1 (0.2%)
5. Imaging modalities			
cUS + PS + 4D-CT + ¹¹ C-methionine PET + ¹⁸ F-choline PET	1 (0.4%)	0	1 (0.2%)
Total	285 (69.3%)	126 (30.7%)	411 (100%)

Note: Criterion adherence = utilization of at least cervical ultrasonography and parathyroid scintigraphy.

Abbreviations: cUS, cervical ultrasonography; PS, parathyroid scintigraphy 4D-CT, four-dimensional computerized tomography.

(OR) with their 95% confidence interval (CI). A *P*-value <.05 was considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics version 25.0 (IBM Corp., Armonk, NY).

3 | RESULTS

3.1 | Study population and baseline characteristics

In total, 411 patients were included in this study (23% male) and the mean age was 61 ± 13 years. Patients' baseline characteristics are depicted in Table 1.

3.2 | Preoperative evaluation.

The mean preoperative total serum calcium was 2.88 ± 0.22 mmol/L ($n = 409$). In 370/411 patients the preoperative albumin-corrected calcium was available, with a mean of 2.82 ± 0.24 mmol/L. Mean preoperative PTH was 24.7 ± 30.1 pmol/L ($n = 402$) (Table 1).

In 298 patients (73%) a preoperative dual-energy X-ray absorptiometry (DXA) was performed, showing osteopenia in 87 patients and osteoporosis in 126 patients.

3.3 | Preoperative imaging

In 285/411 patients (69%) (amongst others) a cUS and PS was performed, as recommended by the guidelines. Of these 285 patients, in the majority ($n = 212$) the preoperative imaging consisted only of cUS and PS, and in 73 patients more imaging modalities were added to the workup (Table 2).

The majority of the 411 included patients had two ($n = 249$) or one ($n = 79$) preoperative imaging modalities. However, in 61 patients three imaging procedure were performed, in 21 patients four imaging techniques, and in 1 patient even five different imaging procedures were deemed necessary. The most performed scan was PS ($n = 399$), followed by cUS ($n = 296$). For further details on preoperative imaging modalities, refer to Table 2.

3.4 | Surgery and pathology

There was no significant difference ($P = .797$) between the percentage of patients that underwent a MIP; in both groups this was in 75% of the patients ($n = 216/285$ in adherence to guidelines and $n = 94/126$ in no adherence) (Table 3, Figure 2). Mean operation time in patients in whom guidelines were followed was 107 ± 52 min vs 118 ± 60 min in whom guidelines were not followed ($P = .066$) (Table 3). The

TABLE 3 Procedural characteristics and outcomes stratified by adherence to consensus criteria

Characteristics	Criterion adherence (n = 285)	Criterion no adherence (n = 126)	Total (n = 411)	P value
MIP No. (% per group)	216 (76%)	94 (75%)	310 (75%)	.797
Operation time, min Mean \pm SD	107 ± 52 (n = 285)	118 ± 60 (n = 126)	110 ± 55 (n = 411)	.066
Adenoma weight, mg Mean \pm SD	1646 ± 2621 (n = 259)	2359 ± 3911 (n = 110)	1859 ± 3075 (n = 369)	.082
Adenoma diameter, mm Mean \pm SD	21.8 ± 20.7 (n = 253)	23.2 ± 12.3 (n = 115)	22.3 ± 18.5 (n = 368)	.514
Multiple gland disease n (% per group)	11 (4%)	4 (3%)	15 (4%)	.733
Days of hospitalization No. (% per group)	179 (63%)	46 (37%)	225 (55%)	<.0005 ^a
≤ 1 ≥ 2	106 (37%)	80 (63%)	186 (45%)	
Normocalcemia ≥ 3 months postoperative No. (% per group)	163 (92%) (n = 178)	80 (91%) (n = 88)	243 (91%) (n = 266)	.856
Cured ≥ 6 months postoperative No. (% per group)	136 (93%) (n = 147)	64 (91%) (n = 70)	200 (92%) (n = 217)	.780
Persistent HPT No. (% per group)	18 (6%)	9 (7%)	27 (7%)	.755
Recurrent HPT No. (% per group)	4 (1%)	1 (1%)	5 (1%)	.603

Note: Criterion adherence = utilization of at least cervical ultrasonography and parathyroid scintigraphy.

Abbreviations: MIP, minimally invasive parathyroidectomy; POD, postoperative day; HPT, hyperparathyroidism; persistent HPT, failure to achieve normocalcemia within 6 months of parathyroidectomy; recurrent HPT, recurrence of hypercalcemia after a normocalcemic interval > 6 months after parathyroidectomy.

^aStatically significant.

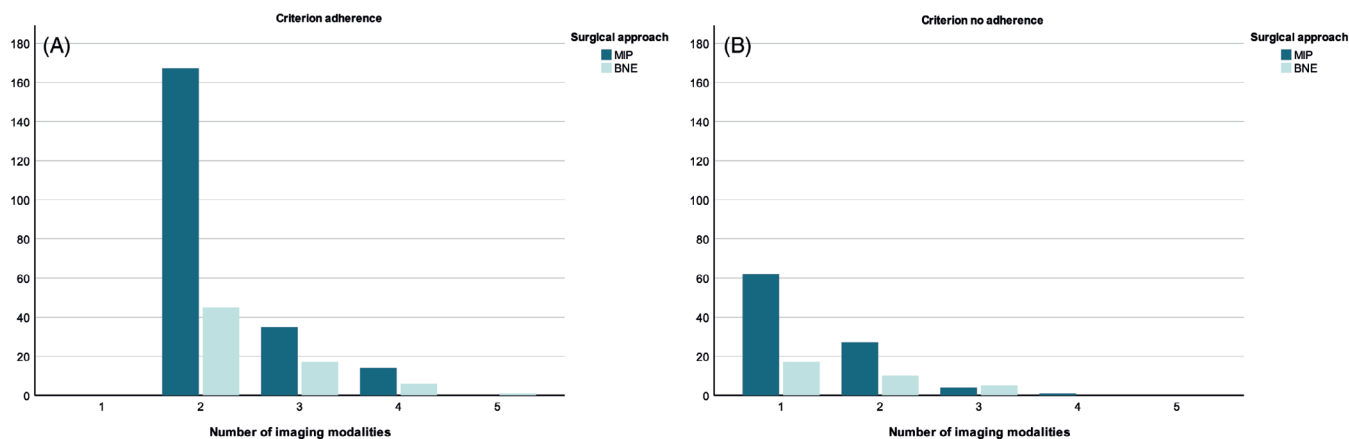


FIGURE 2 Number of patients plotted against the number of imaging procedures combined with the performed surgical approach, also separated for adherence to guidelines (adherence, A, vs no adherence, B). Abbreviations: MIP, minimally invasive parathyroidectomy; BNE, bilateral neck exploration

surgeon used ioPTH in 390 patients (96%) with a sufficient decrease in 92% ($n = 344/373$ [$n = 17$ missing ioPTH values]) of patients (92% for both groups [$P = .944$]). In 11/29 patients (38%) without a sufficient decrease a BNE was performed.

In 93% ($n = 384$) of patients a single parathyroid adenoma was identified by the pathologist, in 3% ($n = 14$) two adenomas and in 0.2% ($n = 1$) three adenomas, totaling 15 patients (4%) with multigland disease (Table 3).

Interestingly, in patients in whom guidelines were followed 63% were discharged within one day vs 37% in whom guidelines were not followed ($P < .0005$) (Table 3). Six months postoperative 92% of patients were cured (93% in adherence to guidelines vs 91% in no adherence [$P = .780$]).

The surgical approach was not influenced by gender (OR .957, 95% CI 0.561-1.633, $P = .873$), BMI (OR 0.979, 95% CI 0.923-1.038, $P = .475$), previous neck surgery (OR 0.862, 95% CI 0.436-1.701, $P = .668$), the year in which the parathyroidectomy was performed (OR 0.933, 95% CI 0.870-1.000, $P = .050$) or by adherence to guidelines on preoperative imaging (utilizing cUS and PS) (OR 1.066, 95% CI 0.657-1.729, $P = .797$). However, the use of a bimodality imaging workup, starting with cUS and PS followed by imaging upscaling aiming for positive anatomical and functional concordance, was a significant predictor for the performance of a MIP (OR 4.098, 95% CI 2.296-7.315, $P < .0005$). This same effect was observed in the multiple logistic regression (OR 4.098, 95% CI 2.296-7.315, $P < .0005$).

4 | DISCUSSION

In this study, we found that adherence to consensus guidelines on preoperative imaging in routine daily practice was suboptimal, as only in 69% of patients a cUS and PS was performed. Overall, we found that in daily care the preoperative imaging workup was managed in a heterogeneous manner and the number of preoperative imaging modalities ranged from one to five. Patients in whom adherence was

achieved showed a shorter duration of hospitalization, and if imaging upscaling was performed aiming for positive concordance of anatomical and functional localization, adherence was associated with the performance of a MIP, as expected.

The composition of the preoperative imaging workup in patients with pHPT has been investigated earlier in survey studies. A survey study among endocrine surgeons in Spain and Portugal showed that the first ordered preoperative tests were cUS and PS.¹¹ Before first-time surgery, only 44% of surgeons ordered additional tests if the initial imaging modalities failed to localize the adenoma.¹¹ Another survey among Spanish hospital endocrinology services showed that localization studies before surgery were routinely performed in 84% of centers.¹² They showed that PS was considered the most essential tool (81%), followed by cUS (70%) and CT (56%). Furthermore, a survey among Swiss endocrinologists in 2007 showed that localization studies consisted of cUS in 93% and PS in 80%. These articles suggest, based on subjective data, that guidelines on the preoperative imaging workup are being followed. To our knowledge, this is the first patient files-based analysis of the degree of adherence to imaging guidelines in routine daily practice.

Adherence to guidelines in real-practice has been studied before by Kuo et al and Yeh et al.^{5,6} However, they specifically focused on the decision for parathyroidectomy in patients with pHPT. These two studies from the United States, one conducted in a university hospital and one in a large secondary referral center, showed adherence of 40%-50% to surgical management guidelines, emphasizing that non-adherence to guidelines is a global problem.^{5,6} Regarding preoperative imaging guidelines, our study showed that in 69% of cases adherence was achieved. This percentage of adherence to guidelines is higher than the adherence described in literature. However, in almost one-third of patients, there was no adherence to the guidelines in this respect.

Furthermore, in only 30% of our patients the 25(OH)D levels were determined, although the AAES guideline recommends that the biochemical evaluation of suspected pHPT should include total serum

calcium, PTH, creatinine, and 25(OH)D levels.³ Determining 25(OH)D levels is crucial in the diagnosis of pHPT since 25(OH)D deficiency can cause increased levels of PTH. In addition, the AAES guideline recommends a DXA scan for all patients with pHPT. In our cohort, DXA was, however, performed in only 73% of patients.

The reasons for non-adherence to the AAES and ESES guidelines are likely multifactorial. A possible explanation may be the lack of widespread knowledge of their existence among physicians. The workup for imaging in pHPT is often already performed by endocrinologists who are not the intended audience of the AAES and ESES guidelines. Therefore, regularly patients are referred to a surgeon when they already have a localization, while preferably, they should already be referred to the surgeon when having a biochemical diagnosis of pHPT. Often endocrinologists use imaging as a selection tool and only refer localized patients, while patients without a localization should also undergo surgery to be cured. It should also be noted that the ESES statement was published in 2009 and the AAES guideline in 2016, and that our study cohort ranged from 2007 to 2017. Furthermore, doctors may implement other guidelines than those proposed by the AAES and ESES, which were not considered in this study. Nevertheless, in retrospect, when the guidelines were followed patients showed a shorter duration of hospitalization, and if imaging upscaling was performed according to the guidelines, this resulted more often in a MIP compared to a BNE. Since in the non-adherence group the majority of patients had PS rather than US, to improve compliance to preoperative imaging guidelines, clinician-performed US may be considered as it is easy, feasible done by the surgeon and performed in the office.

The cure rate at six months postoperative in our cohort (92%) is lower than the mentioned 95% to 99% in the AAES guideline³, which may be due to the retrospective nature of our study, for example, loss to follow-up. Patients that are cured are often referred to their treating physician in a district hospital or to their general practitioner for calcium monitoring, while patients that are not cured are usually not discharged from follow-up. For this reason, the depicted cure rate in this cohort may be underestimated.

Our study has several limitations. First, this study was subjected to a verification bias and had a retrospective design resulting in missing values. Secondly, the described effect of our bimodality imaging workup on the performance of MIP might be biased since we included the imaging results of the initially performed scans (cUS and PS) in our analysis. Lastly, we did not take low dose CT added to functional imaging techniques into account, such as the SPECT/CT or PET/CT. The adenoma might have been detected on both functional imaging as well as on low dose CT, which would prompt anatomical and functional localization. This analysis was not performed since we only evaluated the final imaging reports.

The main strength of our study is that it describes and reflects the current practice of preoperative imaging across hospitals. This allows for a more accurate estimation of adherence to guidelines and demonstrates the impact of non-adherence on the surgical approach and duration of hospitalization. This study could help physicians in requesting localizing imaging modalities. Patients with a biochemical diagnosis of pHPT and an indication for surgery should have a

protocolized preoperative diagnostic workup. The discrepancy between recommended practice and actual clinical practice is striking and warrants better education of physicians regarding the appropriate preoperative imaging workup of pHPT, leading ultimately to an increased appropriate adherence to consensus guidelines.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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