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Diagnostic performance of ultrasound versus 99mTc-sestamibi scintigraphy in preoperative depiction and localization of parathyroid adenoma in patients with primary hyperparathyroidism

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ABSTRACT

Objectives: To evaluate diagnostic performance of ultrasound (US) and 99mTc-sestamibi scintigraphy (MIBI) in preoperative depiction and localization of parathyroid adenoma in patients with primary hyperparathyroidism (PHPT)

Methods: A total of 645 patients (mean age: 52.3 [range; 18-81] years, 72.9% were females) who underwent parathyroidectomy for PHPT due to histopathologically-confirmed adenoma were included in this retrospective cohort study. The accuracy of preoperative US and MIBI in the depiction and localization of parathyroid adenomas was evaluated with respect to intraoperative localization.

Results: Preoperative MIBI was more accurate than preoperative US in identifying upper right (6.2% vs. 2.6%) and upper left (7.5% vs. 3.8%) orthotopic adenomas, and ectopic adenomas (1.5% vs. 0.7%). Failure to identify an adenoma was less commonly noted on preoperative MIBI than on preoperative US (26.9% vs. 32.8%). The US mainly failed to diagnose the adenomas located in the upper left (27.4%), lower left (25.9%) and upper right (19.3%) orthotopic sites, while MIBI mainly missed those located in the lower left (36.2%), lower right (24.7%) and upper left (20.1%) orthotopic sites. True-positive depiction rates on the preoperative US (60.4% for ≤250 mg, 80.3% for ≥901 mg) and MIBI (56.7% for ≤250 mg, 86.7% for ≥901 mg) were increased as the parathyroid weight increased.

Conclusions: Our findings indicate inconclusive results in the identification of parathyroid adenoma in nearly one-third of cases with both US and MIBI and the side-specific and site-specific variations in their performance. Hence, the combined use of these imaging modalities may be of great clinical value in the precise preoperative depiction and localization of parathyroid adenomas.

Keywords: Primary hyperparathyroidism, preoperative imaging, ultrasound, 99mTc-sestamibi scintigraphy, parathyroid adenoma, localization

Primary hyperparathyroidism (PHPT), a common endocrine disorder associated with an overactive parathyroid gland, is caused by a parathyroid adenoma in majority of cases, followed by hyperplasia and rarely carcinoma of the parathyroid gland [1].

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Surgical resection of pathological parathyroid glands via bilateral neck exploration (BNE) or minimally invasive focused parathyroidectomy (MIP) is the only definite treatment for PHPT [2]. Owing to an improved presurgical imaging technology enabling the implementation of a less extensive but similarly effective surgical approach, a dramatic shift has occurred in the surgical practice over the last two decades, with increasing use of MIP over traditional BNE in PHPT patients [2, 3]. Hence, MIP has become the surgery of choice in solitary adenomas, which provides high surgical cure rates along with lower complication rates, shorter surgery duration, and hospital stay, and improved cosmetic results when compared to BNE [4, 5].

Accordingly, preoperative imaging has become increasingly important in clinical practice as the success of MIP is highly dependent on the accurate preoperative detection and localization of abnormal parathyroid lesions [6,7]. Preoperative imaging enables not only the lateralization and the exact location of abnormal glands but also helps the surgeon with the qualification of patients who would be better served with BNE or MIP [4, 5].

The ultrasound (US) and 99mTc-sestamibi scintigraphy (MIBI) are considered the first-line imaging modalities for the preoperative detection and localization of parathyroid adenomas [4, 6-9]. However, the reported sensitivities of neck US and MIBI scans range from 65% to 81.4% and from 61.0% to 90.6%, respectively, and up to 20% of preoperative imaging results are considered inconclusive [4, 8, 10, 11].

Nonetheless, most of the studies addressing the diagnostic performance of preoperative imaging modalities are small scale studies without detailed analysis of adenoma localization (i.e., lateralization or site-specific characteristics) and the optimal preoperative localization technique remains to be inconclusive [6, 8, 10-12].

This retrospective single-center study aimed to comparatively evaluate the performance of preoperative imaging modalities (US and MIBI) in preoperative depiction and localization of parathyroid adenoma in a homogenous surgical cohort of patients with PHPT, using a detailed 4-quadrant side/site-specific analysis.

METHODS

Study population

A total of 645 patients (mean age: 52.3 [range; 18-81] years, 72.9% were females) who underwent parathyroidectomy for PHPT due to histopathologically-confirmed adenoma were included in this single-center retrospective cohort study conducted at a tertiary care general surgery clinic between January 2005 and June

Table 1. Patient demographics, preoperative laboratory findings and surgical approach

Patient demographics	
Age (year), mean (min-max)	52.3 (18-81)
Gender, n (%)	
Female	470(72.9)
Male	175(27.1)
Preoperative laboratory findings, median (min-max)	
Serum calcium (mEq/L)	9.1(8.3-13.2)
Serum PTH (pg/mL)	148(111-1867)
Surgical approach, n (%)	
Minimally invasive focused parathyroidectomy (MIP)	356(55.2)
Bilateral neck exploration (BNE)	289(44.8)
Initial choice	*239(37.1)*
Converted from MIP	*50(7.7)*

PTH=parathyroid hormone

2023. The presence of preoperative US and MIBI reports, and the confirmed postoperative histopathological diagnosis of parathyroid adenoma or hyperplasia were the study's inclusion criteria. Patients without preoperative imaging data (US or MIBI), those without a confirmed histopathological diagnosis of adenoma or hyperplasia, and those with postoperative recurrence or persistence were excluded from the study.

Written informed consent was obtained from each participant. This study was conducted in accordance with the ethical principles stated in the "Declaration of Helsinki" and approved by the Bursa Uludag University Clinical Research Ethics Committee (Date of Approval: 19/09/2023; Protocol No: 2023-17/60).

Assessments

Patient demographics (age, gender), preoperative parathyroid hormone (PTH) and calcium levels, and preoperative imaging data on 4-quadrant adenoma localization were recorded in each patient. The accuracy of preoperative US and MIBI in depiction and localization of parathyroid adenomas was evaluated with respect to intraoperative localization which was defined as a reference of the localization diagnostics. The intraoperative parathyroid adenoma localization and the true-positive US and MIBI depiction rates were also evaluated with respect to parathyroid weight.

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, version 22.0. Armonk, NY: IBM Corp). Descriptive statistics were reported including means and ranges for continuous variables and percentages for categorical variables. Data were expressed as mean, median (minimum-maximum), and percent (%) where appropriate.

RESULTS

Patient Demographics, Preoperative Laboratory Findings, and Surgery Type

The mean patient age was 52.3 (range: 18-81) years, and females composed the 72.9% of the study population. Median levels for preoperative serum calcium and serum PTH were 9.1 (8.3-13.2) mEq/L and 148 (111-1867) pg/mL, respectively (Table 1).

All patients with solitary adenoma detected on preoperative imaging were operated with MIP (n=356, 55.2%), while those with multi-gland disease or suspicious/negative imaging were operated with BNE (n=289, 44.8%). The operation was initially started with MIP but then converted to BNE in 50 of 289 BNE-operated patients (Table 1).

Preoperative Imaging with Respect to Intraoperative Localization

Intraoperative localization revealed that most of parathyroid adenomas were located inferiorly (73.2%)

Table 2. Parathyroid adenoma localization: Preoperative US and MIBI with respect to intraoperative assessment

	Preoperative US (n=645)	Preoperative MIBI (n=645)	Intraoperative findings (n=645)
Adenoma localization, n (%)			
Orthotopic			
Lower left	206 (31.9)	198 (30.8)	261 (40.4)
Lower right	176 (27.2)	169 (25.9)	212 (32.8)
Upper left	25 (3.8)	48 (7.2)	83 (12.8)
Upper right	17 (2.6)	40 (6.2)	58 (8.9)
Ectopic	5 (0.7)	10 (1.5)	19 (2.9)
Bilateral	4 (0.6)	6 (0.9)	12 (1.8)
Not found	212 (32.8)	174 (26.9)	

US=Ultrasound, MIBI=99mTc-sestamibi scintigraphy

Table 3. **Distribution of missed parathyroid adenoma diagnoses by preoperative US (n=212) and MIBI (n=174)**

		Missed diagnoses by preoperative imaging		Intraoperative reference data on localization diagnostics
		Preoperative US	Preoperative MIBI	
Orthotopic, n (%)				
Inferior	Lower left	55 (25.9)	63 (36.2)	261
	Lower right	36 (17.0)	43 (24.7)	212
Superior	Upper left	58(27.4)	35 (20.1)	83
	Upper right	41 (19.3)	18 (10.3)	58
Ectopic, n (%)		14 (6.6)	9 (5.2)	19
Bilateral, n (%)		8 (3.8)	6 (3.5)	12
Total		212 (100.0)	174 (100.0)	

US: Ultrasound; MIBI: 99mTc-sestamibi scintigraphy Shaded areas indicate better performance of the imaging modality

including the lower left (40.4%) or lower right (32.8%) orthotopic sites. Preoperative US and MIBI, although at a lower rate than the intraoperative assessment, identified the lower right (27.2% and. 25.9%) and the lower left (31.9% vs. 30.8%) orthotopic adenomas with similar accuracy (Table 2).

Intraoperatively, only 21.7% of parathyroid adenomas were located superiorly including the upper left (12.8%) or upper right (8.9%) orthotopic sites, while ectopic (2.9%) and bilateral (1.8%) adenomas were the least commonly identified ones (Table 2).

The preoperative MIBI, compared with the preoperative US, was more accurate in identifying adenomas in the less-common localizations such as the

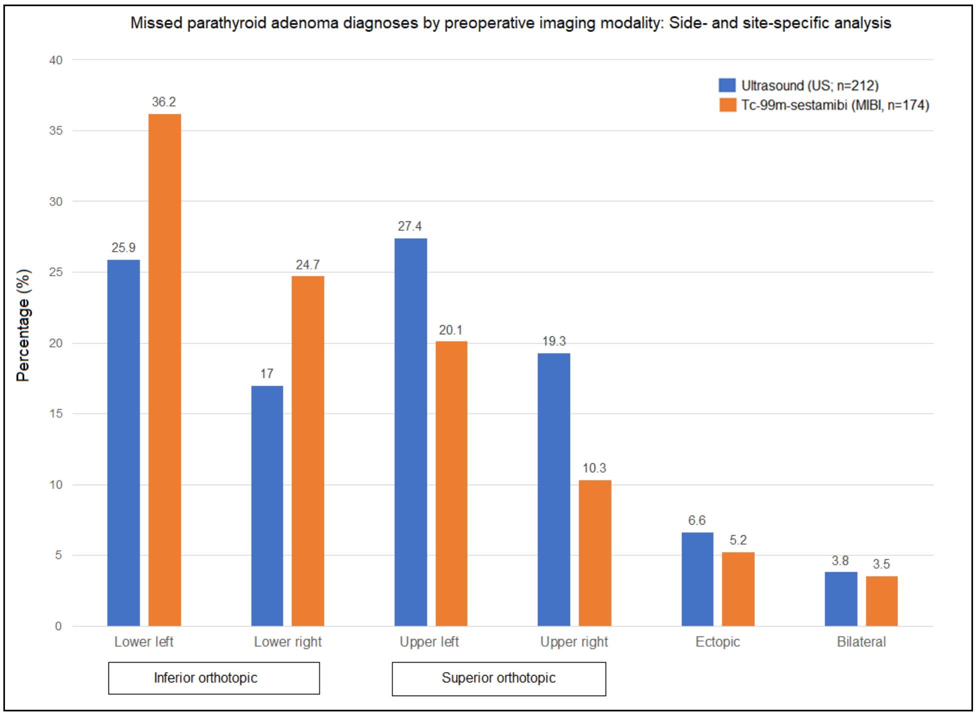

Fig. 1. **Side- and site-specific analysis of the missed parathyroid adenoma diagnosis by preoperative US (n=212) and MIBI (n=174).**

Table 4. Intraoperative localization and true-positive US and MIBI depiction rates according to parathyroid weight

	Parathyroid weight (mg)			
	≤250 mg	251-500 mg	501-900 mg	≥901 mg
Intraoperative parathyroid adenoma localization, n (%)				
Unilateral adenoma (n=614)	**162 (26.4)**	**165 (26.9)**	**151 (24.6)**	**136 (22.1)**
Bilateral adenoma (n=12, total 24)	7 (29.2)	9 (37.5)	5 (20.8)	3 (12.5)
Ectopic adenoma (n=19)	6 (31.6)	7 (36.8)	4 (21.1)	2 (10.5)
True positive depiction on preoperative imaging, n(%)				
True positive US (n=424)	98/162 (60.4%)	104/165 (75.4%)	110/151 (80.1%)	112/136 (80.3%)
True positive MIBI (n=455)	92/162 (56.7%)	118/165 (71.5%)	127/151 (84.1%)	118/136 (86.7%)

US=Ultrasound, MIBI=99mTc-sestamibi scintigraphy

upper right (6.2% vs. 2.6%) and the upper left (7.5% vs. 3.8%) orthotopic adenomas, as well as the ectopic (1.5% vs. 0.7%) adenomas. Failure to locate an adenoma was less commonly noted on preoperative MIBI than on preoperative US (174 missed locations [26.9%] vs. 212 missed locations [32.8%], respectively) (Table 2).

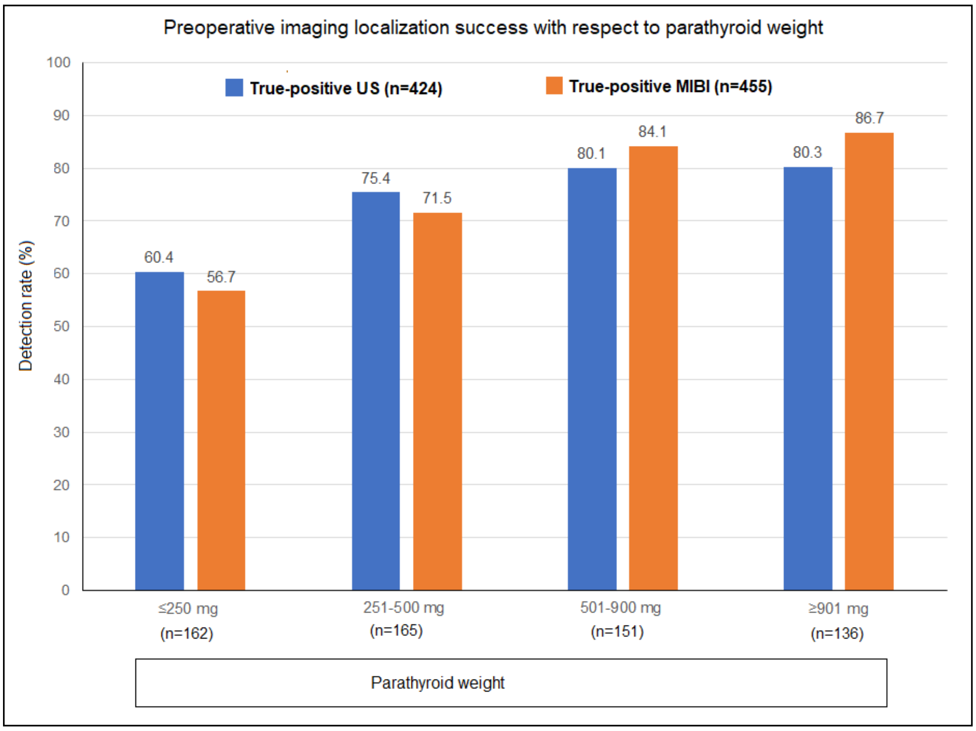

Fig. 2. Preoperative imaging success in localization of adenoma with respect to parathyroid weight.

Distribution of Missed Locations by Preoperative US (n=212) and MIBI (n=174)

Overall, preoperative US mainly missed the adenomas located in the upper left (27.4%), lower left (25.9%) and upper right (19.3%) orthotopic sites. Lower left (36.2%), lower right (24.7%) and upper left (20.1%) orthotopic sites comprised the majority of missed adenoma localizations on preoperative MIBI (Table 3, Fig. 1).

The left-sided adenomas were more disadvantageous than the right-sided adenomas in terms of being recognized on preoperative imaging, regardless of the imaging modality; whereas US more accurately identified the inferiorly located adenomas and MIBI more accurately identified the superiorly located adenomas (Fig. 1).

Intraoperative Localization and True-positive US and MIBI Depiction Rates According to Oarathyroid Weight

Intraoperative findings revealed that parathyroid weight groups were equally presented in unilateral adenoma cases, while parathyroid weight <500 mg was more common than greater parathyroid weights in bilateral and ectopic adenomas (Table 4).

True-positive depiction rates on preoperative US (from 60.4% for ≤250 mg to 80.3% for ≥901 mg) and MIBI (from 56.7% for ≤250 mg to 86.7% for ≥901 mg) were increased as the parathyroid weight increased (Table 4, Fig. 2).

DISCUSSION

In this single-center retrospective study in a homogenous surgical cohort of PHPT patients treated over 18 years, preoperative imaging failed to identify nearly one-third of parathyroid adenomas detected intraoperatively (32.8% by US and 26.9% by MIBI). Regarding intraoperative findings, the US and MIBI modalities showed similar accuracy in correctly identifying the adenomas located in more prevalent anatomic sites (i.e., inferior orthotopic sites). However, their performance differed in less-prevalent anatomic sites (i.e., superior orthotopic sites, ectopic location) in favor of MIBI. Specifically, both the US and MIBI failed to localize primarily the left-sided adenomas, along with a site-specific variation in the risk of a missed diagnosis. This risk of a missed diagnosis was lower with US for the adenomas located in the inferior orthotopic sites and was lower with MIBI for those located in the superior orthotopic sites.

Our intraoperative assessment revealed that most parathyroid adenomas were located inferiorly (73.2%) at the lower left (40.4%) or lower right (32.8%) orthotopic sites, while 21.7% were located superiorly at the upper left (12.8%) and the upper right (8.9%) orthotopic sites and only 2.9% were ectopic adenomas. These findings support the consistently reported preponderance of lower orthotopic sites as the most common parathyroid adenoma location in large series of PHPT patients, including those from Turkey which indicated the lower left location in more than 40% of adenomas [10, 13, 14].

In our cohort, preoperative MIBI was associated with certain advantages over the US such as the lower rate of missed diagnoses overall (26.9% vs. 32.8%, respectively), and more common diagnoses of superiorly located adenomas and ectopic adenomas. Similarly, previous studies from Turkey also indicated the association of MIBI vs. US with a more common detection of single parathyroid adenoma, as well as with a higher sensitivity (70 vs. 60% and 92.17 vs. 75.89%), accuracy (90.9 vs. 87.1% and 87.60 vs. 70.25%) and positive predictive value (PPV; 94.64% vs. 90.43%) in identifying parathyroid adenomas [15, 16]. Also, in a meta-analysis of 12 studies on the performance of preoperative imaging in identifying parathyroid adenomas, the pooled sensitivity of the US and MIBI was found to be similar (83% vs. 80%), while the pooled estimate of MIBI specificity was significantly higher than the US [17].

Indeed, technical advances, such as hybrid Single Photon Emission Computed Tomography/ Computed Tomography (SPECT/CT) acquisition is considered likely to account for the higher sensitivity, specificity, and accuracy of MIBI compared to US, enabling a more precise preoperative depiction of parathyroid adenomas, mainly those in ectopic locations (i.e., retro tracheal, retrosternal, upper mediastinal and intrathymic regions) [4, 6, 9, 11].

Accordingly, in a recent study with 213 PHPT patients, preoperative MIBI SPECT/CT was found to show higher sensitivity (84% vs. 72%) and accuracy (80% vs. 71%) compared to the US, and to enable greater anatomical precision (75.8% vs 68.7%) even in the case of ectopic glands or coexisting thyroid pathology [11].

Moreover, in a recent study by Van den Bruel *et al*. [7] in 104 PHPT patients, the correct identification and misclassification rates by US and MIBI for the upper (70.7% and 48.3% on US; 54.1% and 55.0% on MIBI) and lower (78.7% and 10.4% on US; 59.3% and 2.9% on MIBI) adenomas showed that nearly one-third of superior adenomas detected intraoperatively were called inferior by preoperative imaging. Indeed, in accordance with the embryological development of the parathyroid glands from the branchial pouches, the lower and upper parathyroids are more correctly called P3 and P4, respectively by virtue of cross-migration from the respective pockets, while the superior parathyroid glands growing downwards posteriorly can be mistaken for the lower ones. This upper/lower mispositioning by imaging is suggested to be related to the inability to visualize anatomical landmarks (i.e., the recurrent laryngeal nerve, inferior thyroid artery) as a reference point, by any imaging modality [7, 18]. Considering the risk of misdiagnosis attributable to each preoperative imaging modality, our findings indicate the left-sided orthotopic glands to be less often diagnosed by both US and MIBI, along with higher performance of US for inferiorly located adenomas and that of MIBI for superiorly located and ectopic adenomas. Nonetheless, there is no current universally accepted algorithm for imaging localization in the setting of PHPT, while the studies also revealed controversial data on the overall, and site- or side-specific diagnostic performance of preoperative imaging modalities in PHPT patients.

In a retrospective series of 1089 operated PHPT patients by Iwen *et al*., MIBI and US were associated with failure to identify the gland in 29.8% and 29.4% of patients, respectively, while ectopic and orthotopic upper glands were much less often diagnosed by both MIBI and US [10]. Iwen *et al*. [10] also reported that the sensitivity of US and MIBI was higher for lower left (68.9% and 72%, respectively) adenomas, while their specificity was higher for upper right (99.2% and 99.1%, respectively) adenomas.

Adkisson *et al*. [12] reported the association of both US and MIBI with similarly high rates of accurate preoperative identification of inferiorly located adenomas, whereas a higher rate of accurate adenoma localization by US compared to MIBI (63% vs. 41%). De Simone *et al*. [19] reported the correct detection and failure rates for superior adenomas (56.25% and 43.75% for US and 37.5% and 62.5% for MIBI) and inferior adenomas (86.66% and 13.33% for US and 68.88% and 13.33% for MIBI), indicating higher sensitivity of US for inferior solitary adenoma and lower sensitivity of MIBI for superior adenoma. Other studies also reported higher accuracy (93% vs. 90% and 93 vs. 63%) and sensitivity (98% vs. 93%, 88.0% vs. 63.0% and 91.5 vs. 56.1%) of US vs. MIBI in the preoperative localization of parathyroid adenomas [6, 20].

Nonetheless, for such retrospective series studies over long time periods, the imaging findings are subject to interobserver differences or change in hospital protocols over time [10]. Importantly, there are certain factors affecting the diagnostic accuracy of preoperative imaging for localizing abnormal glands, such as differences in patient population (better performance in SGD than in MGD), differences in imaging acquisition (lower diagnostic accuracy for use of planar scintigraphy imaging alone vs. in combination with SPECT), the method of analysis used for imaging results and surgical reference standards (per-patient or per-lesion/quadrant), concomitant thyroid pathology (decreases US sensitivity), gland weight, the size of adenoma (higher MIBI sensitivity for larger adenomas) and cellular composition of abnormal parathyroid nodules (higher MIBI sensitivity for oxyphil cells) [2, 4-6, 11, 21].

Notably, the association of greater parathyroid weight with increased likelihood of true-positive depiction rates on US (>80% detection rate for weight >501 mg) and MIBI (>86% detection rate for weight >901 mg) in our study supports the impact of the parathyroid weight on the success rate of localization studies with decrease in the localization sensitivity for the minimally enlarged parathyroid adenomas on preoperative imaging [11, 21-24]. Accordingly, previous studies indicated significantly lower parathyroid weights in patients preoperatively mis-localized on US [22], improved MIBI-PS sensitivity when the gland weight is greater than 600 mg [21] as well as significantly higher parathyroid weight in MIBI-positive cases than in MIBI-negative cases (1145.9 mg vs. 692.2 mg) [11].

MIP is the preferred surgical approach in patients with single-gland disease (solitary adenoma) detected on preoperative imaging, while BNE is performed in patients with multi-gland disease (>2 abnormal glands) or with negative imaging [2, 4, 5]. In the current study, the operation was initially started as MIP but then converted to BNE in 50 (7.7%) patients, emphasizing the role of a focused surgical approach even when preoperative imaging modalities indicate a single adenoma, and surgeons should always be prepared to convert from a MIP into BNE if intraoperative findings show multiglandular disease [4, 6, 8, 10, 14].

In fact, given the likelihood of inconclusive results in nearly one-third of PHPT patients by use of US or MIBI alone, and site-specific advantages pertaining to each modality, the combination of both methods may be of great clinical value to obtain the best diagnostic results for precise preoperative visualization of parathyroid adenoma [4, 6, 8, 9, 25]. US-scan is an operator- and instrument-dependent procedure limited to the anterior region of the neck which is also hampered by the concomitant thyroid pathology [4, 9, 25]. However, MIBI-scan, recently integrated with CT-SPECT technique, ranges up to the mediastinum, and is considered an operator-independent procedure less hampered by thyroid enlargement and ideal for ectopic sites [6, 8, 9]. In this regard, the integration of US and MIBI procedures offers greater opportunity for side/site location [4, 6, 8, 9, 25]. Many studies indicated the favorable performance of the combined use of US and MIBI-SPECT/CT in terms of accuracy of preoperative imaging in the setting of PHPT, based on the superiority of MIBI to US in detection of ectopic adenomas, the consideration of US to be useful in cases with low intensity retention of MIBI and the widespread availability and cost-effectiveness of this strategy [4, 6, 8, 9, 26-30].

Limitations

This study has some limitations. First, due to retrospective single-center design, establishing the temporality between cause and effect as well as generalizing our findings to overall PHPT population seems difficult. Second, while the findings were achieved in a homogenous surgical cohort of PHPT patients treated over an 18-year period, inter-operator variability in radiological imaging is another potential limitation with likely effects on results. Third, inability to assess the potential impact of imaging studies on the surgical approach, due to retrospective design, as well as the likelihood of overestimated preoperative imaging performance due to inclusion of only surgical patients are other limitations.

CONCLUSION

In conclusion, this retrospective analysis in a homogenous surgical cohort of PHPT patients revealed the association of preoperative imaging modalities with inconclusive results regarding the identification of parathyroid adenoma in nearly one-third of cases. Left-sided orthotopic glands were less often diagnosed by both US and MIBI, along with higher performance of US for inferiorly located adenomas and that of MIBI for superiorly located adenomas as well as ectopic adenomas. Given the side-specific and site-specific variations in the performance of each imaging modality, our findings emphasize the likelihood of combined use of both modalities to be of great clinical value in the precise preoperative depiction and localization of parathyroid adenomas in patients with PHPT.

Ethics Committee Approval

Written informed consent was obtained from each participant. This study was conducted in accordance with the ethical principles stated in the “Declaration of Helsinki” and approved by the Bursa Uludag University Clinical Research Ethics Committee (Date of Approval: 19/09/2023; Protocol No: 2023-17/60).

Authors’ Contribution

Study Conception: EG; Study Design: EG; Supervision: EG; Funding: N/A; Materials: EG; Data Collection and/or Processing: EG; Statistical Analysis and/or Data Interpretation: EG; Literature Review: EG; Manuscript Preparation: EG and Critical Review: EG.

Conflict of interest

The author disclosed no conflict of interest during the preparation or publication of this manuscript.

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REFERENCES

1. Masi L. Primary Hyperparathyroidism. Front Horm Res. 2019;51:1-12. doi: 10.1159/000491034.
2. Wilhelm SM, Wang TS, Ruan DT, et al. The American Association of Endocrine Surgeons Guidelines for Definitive Management of Primary Hyperparathyroidism. JAMA Surg. 2016;151(10):959-968. doi: 10.1001/jamasurg.2016.2310.
3. Ahmadieh H, Kreidieh O, Akl EA, El-Hajj Fuleihan G. Minimally invasive parathyroidectomy guided by intraoperative parathyroid hormone monitoring (IOPTH) and preoperative imaging versus bilateral neck exploration for primary hyperparathyroidism in adults. Cochrane Database Syst Rev. 2020;10(10):CD010787. doi: 10.1002/14651858.CD010787.pub2.
4. Tay D, Das JP, Yeh R. Preoperative Localization for Primary Hyperparathyroidism: A Clinical Review. Biomedicines. 2021;9(4):390. doi: 10.3390/biomedicines9040390.
5. Udelsman R, Åkerström G, Biagini C, et al. The surgical management of asymptomatic primary hyperparathyroidism: proceedings of the Fourth International Workshop. J Clin Endocrinol Metab. 2014;99(10):3595-3606. doi: 10.1210/jc.2014-2000.
6. Lu R, Zhao W, Yin L, et al. Efficacy of ultrasonography and Tc-99m MIBI SPECT/CT in preoperative localization of parathyroid adenomas causing primary hyperthyroidism. BMC Med Imaging. 2021;21(1):87. doi: 10.1186/s12880-021-00616-1.
7. Van den Bruel A, Bijnens J, Van Haecke H, et al. Preoperative imaging for hyperparathyroidism often takes upper parathyroid adenomas for lower adenomas. Sci Rep. 2023;13(1):7568. doi: 10.1038/s41598-023-32707-0.
8. Szczepanek-Parulska E, Filipowicz D, Czepczyński R, et al. Clinical, Biochemical, and Sonographic Factors Influencing Performance of Parathormone Washout Measurement vs. 99mTc-MIBI Scintigraphy in the Preoperative Diagnostics of Parathyroid Adenomas. J Clin Med. 2023;12(12):4097. doi: 10.3390/jcm12124097.
9. Tawfik AI, Kamr WH, Mahmoud W, Abo Shady IA, Mohamed MH. Added value of ultrasonography and Tc-99m MIBI SPECT/CT combined protocol in preoperative evaluation of parathyroid adenoma. Eur J Radiol Open. 2019;6:336-342. doi: 10.1016/j.ejro.2019.11.002.
10. Iwen KA, Kußmann J, Fendrich V, Lindner K, Zahn A. Accuracy of Parathyroid Adenoma Localization by Preoperative Ultrasound and Sestamibi in 1089 Patients with Primary Hyperparathyroidism. World J Surg. 2022;46(9):2197-2205. doi: 10.1007/s00268-022-06593-y.
11. Blanco-Saiz I, Goñi-Gironés E, Ribelles-Segura MJ, et al. Preoperative parathyroid localization. Relevance of MIBI SPECT-CT in adverse scenarios. Endocrinol Diabetes Nutr (Engl Ed). 2023;70 Suppl 2:35-44. doi: 10.1016/j.endien.2022.11.025.
12. Adkisson CD, Koonce SL, Heckman MG, Thomas CS, Harris AS, Casler JD. Predictors of accuracy in preoperative parathyroid adenoma localization using ultrasound and Tc-99m-Sestamibi: a 4-quadrant analysis. Am J Otolaryngol. 2013;34(5):508-516. doi: 10.1016/j.amjoto.2013.05.001.
13. Bijnens J, Van den Bruel A, Vander Poorten V, et al. Retrospective real-life study on preoperative imaging for minimally invasive parathyroidectomy in primary hyperparathyroidism. Sci Rep. 2022;12(1):17427. doi: 10.1038/s41598-022-18219-3.
14. Demir B, Binnetoglu A, Sahin A, Yavuz DG. Single Center Experience in the Surgical Management of Primary Hyperparathyroidism. Clin Exp Otorhinolaryngol. 2020;13(3):285-290. doi: 10.21053/ceo.2019.01361.
15. Ozkaya M, Elboga U, Sahin E, et al. Evaluation of conventional imaging techniques on preoperative localization in primary hyperparathyroidism. Bosn J Basic Med Sci. 2015;15(1):61-66. doi: 10.17305/bjbms.2015.207.
16. Okudan B, Seven B, Coskun N, Albayrak A. Comparison between single-photon emission computed tomography/computed tomography and ultrasound in preoperative detection of parathyroid adenoma: retrospective review of an institutional experience. Nucl Med Commun. 2019;40(12):1211-1215. doi: 10.1097/MNM.0000000000001104.
17. Nafisi Moghadam R, Amlelshahbaz AP, Namiranian N, et al. Comparative diagnostic performance of ultrasonography and 99mTcsestamibi scintigraphy for parathyroid adenoma in primary hyperparathyroidism; systematic review and meta- analysis. Asian Pac J Cancer Prev. 2017;18(12):3195-3200. doi: 10.22034/APJCP.2017.18.12.3195.
18. Moreno MA, Callender GG, Woodburn K, et al. Common locations of parathyroid adenomas. Ann Surg Oncol. 2011;18(4):1047-1051. doi: 10.1245/s10434-010-1429-x.
19. De Simone B, Del Rio P, Catena F, et al. Preoperative localization of parathyroid adenoma in video-assisted era: is cervical ultrasound or 99mTc Sesta MIBI scintigraphy better? Minerva Chir. 2017;72(5):375-382. doi: 10.23736/S0026-4733.17.07359-X.
20. Kaur P, Gattani R, Singhal AA, Sarin D, Arora SK, Mithal A. Impact of preoperative imaging on surgical approach for primary hyperparathyroidism: Data from single institution in India. Indian J Endocrinol Metab. 2016;20(5):625-630. doi: 10.4103/2230-8210.190540.
21. Acín-Gándara D, Pereira-Pérez F, Medina-García M, Sebastián-Viana Tomás. Factors influencing the sensitivity of ultrasound and gamma location of the parathyroid adenoma. Cir Esp (Engl Ed). 2020;98(1):18-25. doi: 10.1016/j.ciresp.2019.09.002.
22. Kocaöz S, Yazıcıoğlu MÖ, Çomçalı B, et al. Use of preoperative ultrasonography adenoma size measurements for accurate localization estimation in parathyroid adenomas. Arch Curr Med Res. 2024;5(1):28-35. doi: 10.47482/acmr.1325481.
23. Stucken EZ, Kutler DI, Moquete R, Kazam E, Kuhel WI. Localization of small parathyroid adenomas using modified 4-dimensional computed tomography/ultrasound. Otolaryngol Head Neck Surg. 2012;146(1):33-39. doi: 10.1177/0194599811427243.
24. Keidar Z, Solomonov E, Karry R, Frenkel A, Israel O, Mekel M. Preoperative [99mTc]MIBI SPECT/CT interpretation criteria for localization of parathyroid adenomas-correlation with surgical findings. Mol Imaging Biol. 2017;19(2):265-270. doi: 10.1007/s11307-016-1013-2.
25. Özdemir E, Genç M, Aydos U, et al. Comparison of 99mTc-MIBI planar scintigraphy, SPET/CT and ultrasonography in detection of parathyroid adenoma in patients with primary hyperparathyroidism. Hell J Nucl Med. 2020;23(1):21-26. doi: 10.1967/s002449912002.
26. Zafereo M, Yu J, Angelos P, et al. American Head and Neck

Society Endocrine Surgery Section update on parathyroid imaging for surgical candidates with primary hyperparathyroidism. Head Neck. 2019;41(7):2398-2409. doi: 10.1002/hed.25781.
27. Assante R, Zampella E, Nicolai E, et al. Incremental Value of Sestamibi SPECT/CT Over Dual-Phase Planar Scintigraphy in Patients with Primary Hyperparathyroidism and Inconclusive Ultrasound. Front Med (Lausanne). 2019;6:164. doi: 10.3389/fmed.2019.00164.
28. Patel CN, Salahudeen HM, Lansdown M, Scarsbrook AF. Clinical utility of ultrasound and 99mTc sestamibi SPECT/CT for preoperative localization of parathyroid adenoma in patients with primary hyperparathyroidism. Clin Radiol. 2010;65(4):278-287. doi: 10.1016/j.crad.2009.12.005.
29. Castellana M, Virili C, Palermo A, Giorgino F, Giovanella L, Trimboli P. Primary hyperparathyroidism with surgical indication and negative or equivocal scintigraphy: safety and reliability of PTH washout. A systematic review and meta-analysis. Eur J Endocrinol. 2019;181(3):245-253. doi: 10.1530/EJE-19-0160.
30. Kuzminski SJ, Sosa JA, Hoang JK. Update in Parathyroid Imaging. Magn Reson Imaging Clin N Am. 2018;26(1):151-166. doi: 10.1016/j.mric.2017.08.009.