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REVIEW

False-negative 99mTc-sestamibi scans: factors and outcomes in primary hyperparathyroidism

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Abstract

Primary hyperparathyroidism has emerged as a prevalent endocrine disorder in clinical settings, necessitating in most cases, surgical intervention for the removal of the diseased gland. This condition is characterised by overactivity of the parathyroid glands, resulting in excessive parathyroid hormone production and subsequent disturbances in calcium homeostasis. The primary mode of management is surgical treatment, relying on the accurate localisation of the pathological parathyroid gland. Precise identification is paramount to ensuring that the surgical intervention effectively targets and removes the diseased gland, alleviating the hyperfunctioning state. However, localising the gland becomes challenging, as discrepancies between the clinical manifestation of active parathyroid and radiological identification are common. Based on our current knowledge, to date, no comprehensive review has been conducted that considers all factors collectively. This comprehensive review delves into the factors contributing to false-negative 99mTc-Sestamibi scans. Our research involved an exhaustive search in the PubMed database for hyperparathyroidism, with the identified literature meticulously filtered and reviewed by the authors. The results highlighted various factors, including multiple parathyroid diseases, nodular goitre, mild disease, or the presence of an ectopic gland that causes discordance. Hence, a thorough consideration of these factors is crucial during the diagnostic workup of hyperparathyroidism. Employing intraoperative PTH assays can significantly contribute to a successful cure of the disease, thereby providing a more comprehensive approach to managing this prevalent endocrine disorder.

Keywords: 99mTc-Sestamibi scan; false-negative scans; multi-glandular disease; primary hyperparathyroidism; scan discordance

Introduction

Primary hyperparathyroidism (PHPT) has been recognised as a disease since its first occurrence in Europe and the United States during the 1920s. It is the most common cause of hypercalcaemia in outpatient settings (1). The detection of hyperparathyroidism (HPT) has risen considerably in recent decades due to the widespread availability of medical resources and routine testing of calcium levels. However, vague symptoms may delay identification, diagnosis, and timely management. Proper management is crucial in the early stages to reduce potential morbidities associated with untreated PHPT (2, 3).

The incidence of PHPT is approximately 28 cases per 100,000 individuals in the general population, with the highest occurrence between 50 and 60 years of age. It affects 2% of the population aged 55 years or older and is two to three times more frequent in females (4). Various underlying causes of HPT exist, with single-gland parathyroid adenoma being the most common

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cause (80–87%), followed by multi-glandular disease (glandular hyperplasia in 10–15% of cases or multiple parathyroid adenomas in 2–5% of cases). Parathyroid carcinoma is a rare cause, accounting for less than 5% of all cases of HPT (5).

Accurate pre-operative localisation of the overactive gland(s) is essential since surgical resection is the only curative modality. Appropriate management of HPT relies on proper pre-operative localisation, enhancing focused parathyroidectomy (FP) with minimal postoperative complications (6, 7). A methoxyisobutylisonitrile (MIBI) scan is the imaging modality of choice for localising abnormal parathyroid glands. MIBI contains sestamibi molecules that are not uptaken by normal parathyroid glands; however, overactive parathyroid tissues rapidly uptake these molecules due to the high affinity of abnormal mitochondria to sestamibi, thereby enhancing the overall sensitivity of the MIBI scan, which ranges from 70% to 85% (8, 9, 10). Ultrasound scan (USS)-guided parathyroid biopsy and washout of parathyroid hormone (PTH) may enhance gland detection. False-negative (FN) MIBI scans represent a significant risk to surgical success. Multiple factors contribute to MIBI sensitivity, including gland size, multi-glandular disease, histopathological variants, diseased gland location, the severity of hypercalcemia, and vitamin D levels (11).

Articles published in English from 1993 to March 2024 were searched on PubMed using the medical subject heading (MeSH) terms 'primary hyperparathyroidism', 'negative sestamibi', or 'negative MIBI scan', with suitable Boolean operators. Only primary sources that discussed surgically confirmed parathyroid gland pathology but had negative pre-operative imaging studies were reviewed. The data included USS and MIBI parathyroid scans alongside biochemical data, with recorded post-resection gland weights to evaluate their impact on pre-operative localisation. Secondary sources, such as review articles and studies lacking surgical confirmation or indicating active parathyroid lesions on pre-operative imaging, were excluded. Following full-text assessment, 89 articles were included in the review, but not all references were cited to avoid excessive length and redundancy, as the ideas were often repetitive (Fig. 1). This review evaluates the pre-operative characteristics, biochemical and histopathological factors of patients with PHPT presenting with negative MIBI scans and discordant imaging studies, as well as the surgical outcomes and physicians' attitudes towards these patients.

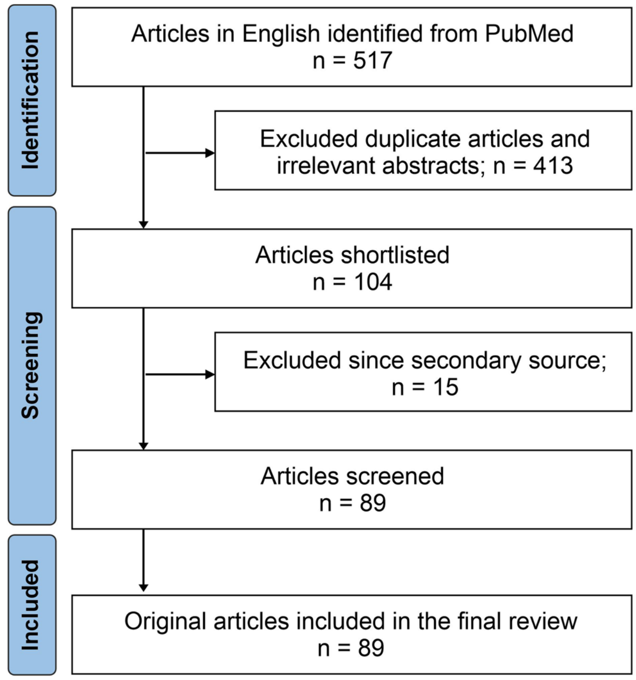

Figure 1

Flow diagram of literature search and study selection for the review.

Factors affecting MIBI scan sensitivity

Accurate diagnostic tools are pivotal for effective patient management. Several factors can influence the sensitivity of MIBI scans, potentially affecting their ability to accurately identify abnormal parathyroid tissue. Understanding these factors is essential for clinicians to interpret MIBI scan results effectively, optimise diagnostic accuracy, and tailor treatment strategies accordingly. This section discusses the multifaceted aspects influencing MIBI scan sensitivity in PHPT, offering insights for informed clinical decision-making.

Multi-glandular disease

Several reports link parathyroid multi-glandular defects with FN pre-operative scans (12, 13, 14, 15). One study categorised participants into groups based on imaging results, revealing operative success rates of 99.12%, 98%, and 90.91% in the MIBI-positive/USS-positive, MIBI-positive/USS-negative, and MIBI-negative/USS-negative groups, respectively, with varying incidences of multi-glandular disease (3.5%, 12%, and 9.09%, respectively) (14). Another study corroborated these findings, reporting multi-glandular disease incidences of 31–40% when both MIBI and USS were negative (12). In a tertiary care centre, a prospective analysis of PHPT surgeries found that positive MIBI scans correlated with higher rates of single-gland disease compared to negative scans, which showed higher rates of multi-glandular defects (87% vs 63%) (16). Patients with negative pre-operative localisation faced a significantly higher risk of multi-glandular disease compared to those with positive results (31.6% vs 3.6%; $P < 0.0001$) (13). Intraoperative PTH (iOPTH) monitoring influenced surgical approaches in cases with

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incorrect or negative scans, preventing unnecessary exploration with a successful excision rate of 97% (17). Challenging common perceptions, a study found that the majority of patients with negative MIBI scans had parathyroid adenoma as the primary cause, rather than hyperplasia (18).

Co-existent thyroid disease

Co-existing thyroid diseases are also potential factors contributing to discordance between scans, reducing the diagnostic accuracy of both USS and MIBI (USS: 71.4% sensitivity, 78.9% specificity; MIBI: 35.7% sensitivity, 42.1% specificity), possibly due to FN results (predominantly in autoimmune thyroid disease) and false-positive results (mainly in nodular goitre) (19). A retrospective review of patients with PHPT showed varying sensitivities and positive predictive values (PPV) for sestamibi combined with pertechnetate (72% and 90%, respectively) and USS (50% and 80%, respectively). Sensitivity and PPV dropped when using sestamibi with pertechnetate in patients with thyroiditis (53% and 77%, respectively) compared to USS (54% and 88%, respectively). However, the presence of thyroid nodules did not affect the sensitivity or PPV for both modalities (20). A decrease in MIBI sensitivity was shown in a study involving patients requiring thyroidectomy due to thyroid nodular disease compared to those not needing thyroidectomy (54.5% vs 73%, respectively) (21). This discordance underscores the importance of fine-needle aspiration and PTH washout as gold-standard diagnostic tools for HPT.

Gland size, histopathology findings, mitochondrial content, and fat cell content

Gland size significantly affects pre-operative scans, with larger adenomas more likely to yield positive results (22, 23, 24). Studies have indicated that excised parathyroid tissue from PHPT cases with negative scans tends to be smaller than those with positive scans (22, 23). Additionally, adenomas with equivocal MIBI scans are smaller and have lower PTH levels than those with positive scans (24). Positive MIBI scans are more common with increased adenoma weights than negative MIBI scans (median: 1180 mg vs 517 mg, $P < 0.05$), while negative MIBI scans are more incidental with hyperplasia than positive MIBI scans (7.7% vs 3.9%, $P < 0.05$) (16). Patients with negative scans tend to have smaller adenomas (mean (s.d.) diameter: 1.3 (0.5) cm vs 1.9 (1.1) cm; $P = 0.008$, mean (s.d.) volume: 0.30 (0.20) cm^3 vs 1.2 (1.1) cm^3; $P < 0.001$, mean (s.d.) weight: 567 (282) mg vs 1470 (1374) mg; $P = 0.030$), predominantly located in the upper region, compared to those with positive scans (65% vs 16%; $P < 0.001$) (25). Similarly, a significantly lower mean gland weight was associated with FN scans compared to true-positive (TP) cases (451 mg vs 1283 mg, $P = 0.005$) (26).

Adenoma weight (>600 mg) and oxyphil content (>20%) were found to significantly influence positive scan results, with FN scans more likely in patients with enlarged parathyroids containing a high proportion of clear cells (27). An immunohistochemical examination revealed hyperplasia glands containing fat were smaller than fat-free glands ($P = 0.009$). However, the proportion of adipose tissue in parathyroid hyperplastic lesions was notably higher in the FN MIBI scan group than in the TP group, although not statistically significant ($P = 0.15$). Elevated levels of Bcl-2 expression were observed in the TP group compared to the FN group, contradicting expected pathophysiological trends. Bcl-2, an anti-apoptotic protein crucial for preserving the integrity of the outer mitochondrial membrane and impeding mitochondrial membrane permeabilisation, thereby inhibiting tracer uptake, was anticipated to hinder tracer accumulation (28). Patients with negative imaging had a higher proportion of chief cells, while patients with positive imaging had a higher incidence of oxyphil cells (16, 29). Parathyroid cells having densely packed mitochondrial content were associated with heightened MIBI scan uptake, while negative MIBI scan uptake was associated with chief cells displaying lower to moderate mitochondrial content (10). This contradicted the results of another study, which revealed that despite the significant mitochondrial content of parathyroid adenoma, the absence of oxyphil cells leads to negative MIBI scanning, possibly due to diminished binding sites (30). Thus, chief cells were predominant in negative imaging, while oxyphil cells were more prevalent in positive imaging. Hyalinisation differences between MIBI-positive and MIBI-negative scans suggest potential mechanisms involving the isolation of cells from fibrous parathyroid tissue, possibly preventing radiotracer uptake (31).

Drug metabolism transporters

In patients with PHPT, drug metabolism transporters like p-glycoprotein (P-gp) disrupt MIBI tracer retention in parathyroid glands. Higher P-gp expression is observed in cases with negative MIBI results, while positive results show low or no P-gp expression (32). Large parathyroid adenomas (>1.5 g) with P-gp or multidrug resistance-related protein (MRP) expression exhibited reduced detection rates on MIBI scans, whereas those negative for both were consistently detected (33). Significant uptake by adenomas with negative P-gp expression suggests that P-gp facilitates radiotracer elimination, contributing to FN results in large tumours (34). Possibly, P-gp or MRP expression in the parathyroid gland acts as a drug efflux pump, potentially facilitating radiotracer elimination in MIBI scans and contributing to FN results in large parathyroid tumours.

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Parathyroid adenoma consistency

Cystic parathyroid adenomas can yield negative MIBI results (35). A case report of a 43-year-old female with a palpable cervical mass suspected of thyroid cancer revealed PHPT. Imaging tests were negative, but iOPTH dropped post-thyroidectomy. Surgical exploration failed to identify the adenoma. Histopathology confirmed the lesion was a partially solid and cystic parathyroid lesion that mimicked thyroid cancer, suggesting apoptosis or necrosis that reduced uptake (36). Diminished cellular density within cystic regions may generate FN MIBI outcomes (35).

Location of parathyroid adenoma

Effective pre-operative localisation is vital for targeted neck exploration in patients with PHPT. Rare occurrences, such as undescended parathyroid adenomas positioned at least 1 cm above the thyroid gland's uppermost aspect, contribute to failed cervical explorations, comprising 0.08% of adenomas and 7% of unsuccessful surgeries (37). Additionally, intra-thyroidal parathyroid adenomas (ITPAs) pose challenges, occurring in 0.5–4.3% of cases, often necessitating advanced imaging like 4D-MRI or choline/PET-CT scans for accurate detection (38, 39). Cases illustrated diverse challenges, such as a carotid sheath adenoma leading to hoarseness and coughing despite a negative MIBI scan, which was resolved post-surgery (40). Another case involved persistent symptoms post-neck exploration, later attributed to a mass near the submandibular gland, emphasising the necessity of thorough investigation (41). Occurrences of a PTH-secreting thymoma and cervical parathyroid adenoma that complicated diagnosis or required multiple surgeries were rarely seen (42). Studies reported increased ectopic parathyroid tumours in patients with negative MIBI scans, guiding surgical approaches due to the higher risk of multi-gland disease. Ectopic parathyroid glands were identified more frequently in patients with positive MIBI scans (43). Embryological insights shed light on ectopic parathyroid gland positions. Inferior parathyroids, along with the thymus, originate from the third pharyngeal pouch, while the superior parathyroids derive from the fourth pouch (44). Undescended parathyroid glands are believed to occur due to the halting of descent of the third pharyngeal pouch, while ectopic parathyroid glands are more common with the inferior parathyroids due to their lengthier descent migratory tract during embryonic development. The prevalent sites of ectopic parathyroid glands, responsible for influencing surgical planning, include the retropharyngeal region, thymus, mediastinum, and intra-thyroidal regions (45). Superior parathyroids are often found ectopically within the tracheo-oesophageal groove (~45%), retro-esophageal region (~20%), or posterior mediastinum (~15%) (44). In contrast, inferior parathyroids are most frequently situated within the thymus (~30%), anterior mediastinum (~20%), intra-thyroidal region (~20%), or at the thyrohyoid ligament (~15%) (44).

Effect of vitamin D level

In a retrospective study involving patients diagnosed with PHPT, serum vitamin D levels did not affect the specificity, sensitivity, or accuracy of MIBI scans for localising parathyroid adenomas. Although vitamin D deficiency was linked to a higher volume of resected adenomas, it did not impact the visualisation of adenomas on MIBI scans (46). Another study on patients with low vitamin D levels (<50 nmol/L) found that combining the results of MIBI scans with high PTH levels (twice the average value) increased the scan specificity from 80% to 93% (47). Thus, combining MIBI analysis with high PTH levels may enhance specificity in patients with low vitamin D levels.

Effect of calcium channel blockers

Calcium channel blockers (CaCBs) may reduce parathyroid cell uptake in MIBI scans. A retrospective analysis of patients with PHPT who underwent surgery revealed that 23% of individuals with negative MIBI SPECT scans were using CaCBs, compared to 14% of those with positive scans. Upon adjusting for age, gender, and gland weight, the odds ratio (OR) revealed a higher likelihood of having a negative scan among those using CaCBs compared to non-users (OR 2.88, 95% CI, 1.03–8.10; P = 0.045) (48).

Correlation of biochemical profile and MIBI scan

Establishing a link between the biochemical profile and MIBI scans is paramount for accurate diagnosis and treatment planning. While biochemical markers such as serum calcium and PTH levels provide valuable insights into disease severity, MIBI scans offer visualisation of parathyroid adenomas, aiding in localisation and surgical decision-making. Insight into the relationship between these diagnostic modalities is essential for clinicians to optimise patient management strategies effectively.

Association with positive scans

The association between a positive MIBI scan and various direct and derived biochemical variables has been extensively studied (8, 23, 49). Patients with a positive scan typically exhibited lower serum phosphate levels and higher PTH levels than those with negative scans (8). Lower calcium and PTH levels also significantly correlated with reduced sensitivity of MIBI scans. While precise cut-off levels of serum calcium and PTH

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for predicting a positive scan are not well-established, plasma calcium levels above 11.3 mg/dL are associated with positive MIBI scans compared to lower values (8, 49). Furthermore, in females, increasing serum PTH levels significantly correlated with a positive MIBI scan, whereas this correlation was insignificant in males (23).

Negative scans and pre-operative calcium levels

The impact of negative pre-operative MIBI scans on the management and surgical outcomes of patients with PHPT remains a subject of significant interest and investigation. A study involving patients undergoing surgery for PHPT after pre-operative MIBI scans revealed that 5.7% had negative MIBI imaging results (50). The group with negative MIBI scans exhibited similar calcium levels (10.9 mg/mL vs 11.0 mg/mL, P = 0.02) but significantly lower urinary calcium levels (251 mg/mL vs 287 mg/mL, P = 0.02) than those with positive scans. However, there were no differences in PTH or vitamin D levels between the two groups. Notably, a curative operation was performed in a lower percentage of patients with negative MIBI scans compared to those with positive scans. Patients who underwent successful surgery despite a negative MIBI scan had similar calcium levels but lower PTH levels compared to those who did not (50). Patients with normal pre-operative calcium levels reported a higher probability of an FN MIBI scan, which was associated with a smaller parathyroid gland and a higher rate of hyperplasia (51).

Surgical outcomes of MIBI-negative scans

Assessing the surgical outcomes of patients with MIBI-negative scans is crucial for perceiving the effectiveness of surgical intervention and guiding postoperative management. While MIBI scans serve as a valuable tool for localising parathyroid adenomas preoperatively, their negative findings pose challenges in surgical planning and predicting outcomes. However, it is important to note that the decision to perform parathyroidectomy is based on a comprehensive evaluation of various modalities, including neck ultrasonography and enhanced CT scans. Although MIBI results contribute to this decision-making, the detailed exploration of other imaging modalities is beyond the scope of this paper.

The outcomes of MIBI-negative scans in patients undergoing parathyroidectomy for PHPT are:

Impact on cure rate

The surgical outcomes of MIBI-negative scans significantly affect the cure rate. When MIBI scans fail to detect abnormalities, there is a heightened risk of incomplete resection during surgery, potentially leading to residual tumour tissue and compromised treatment efficacy. Pre-operative MIBI scanning is thought to enhance the cure rate before parathyroidectomy. A negative MIBI scan may indicate a lack of identifiable parathyroid adenomas, influencing the decision-making process regarding surgical intervention. Accurate preoperative imaging is paramount to ensure optimal surgical outcomes and long-term management of primary hyperparathyroidism. However, contrasting findings exist regarding its impact. While pre-operative MIBI scanning may not alter surgical outcomes, it can help identify patients with lower cure rates, necessitating further exploration. The impact of MIBI-negative scans on surgical outcomes is summarised in Table 1.

Role of iOPTH in MIBI-negative cases

Studies highlight the efficacy of iOPTH, aiding in successful outcomes, particularly in challenging scenarios like MIBI-negative cases (15). In one study involving patients with discordant or negative results, iOPTH facilitated a minimally invasive approach in 72.9% of patients, reducing the incidence of persistent disease (52). Limited parathyroid exploration guided by iOPTH achieved a high cure rate (94.3%) in PHPT patients with negative MIBI scans (53). Using iOPTH significantly improved cure rates, reduced persistent PHPT risk (from 26% to 8%), and decreased the risk of medically treated hypocalcaemia (from 16% to 8%), as seen after a 6-week follow-up (22). While a decrease in iOPTH level predicts success, its positive predictive value is lower in negative imaging cases due to the higher incidence of multi-glandular disease. Thus, continued surgical exploration is advised in patients with negative imaging to ensure thorough resection (29).

Role of gamma probe in scan negative cases

In patients with negative scans, intraoperative gamma probe utilisation, following pre-operative MIBI injection, proves advantageous for localising parathyroid adenomas. A study involving 132 parathyroidectomies, including patients with PHPT and negative MIBI scans, demonstrated a gamma probe sensitivity of 90.5% in identifying adenomas intraoperatively without any false positives, as confirmed by frozen section analysis of resected tissue (54). Moreover, a >50% reduction in iOPTH levels was observed in all but three cases, aligning with the effectiveness of the gamma probe in adenoma localisation.

Physicians' perspective of negative MIBI scans

Negative MIBI scans significantly influence the treatment decisions of both endocrinologists and surgeons, impacting patient referrals and recommendations

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Table 1 Studies related to MIBI-negative scans and surgical outcomes.

Study (Reference)	**Study design**	**Study objective**	**Imaging in patients with PHPT**	**Outcome**
Elaraj *et al.* 2010 (43)	Prospective analysis	Imaging study accuracy and its role in biochemical cure	Pre-operative MIBI scan ($n = 492$)	A higher cure rate is reported in patients with positive MIBI scans (97% vs 89%)
Shen *et al.* 1997 (57)	Retrospective review	MIBI scan accuracy assessment to perform UNE for initial parathyroidectomy	Group 1: Single adenomas ($n = 28$) Group 2: Multiple adenomas ($n = 9$) Group 3: Hyperplasia ($n = 3$)	Accuracy of MIBI scans in disease detection – Group 1: 71% Group 2: 44% Group 3: 0%
Unlu *et al.* 2023 (58)	Retrospective study	Negative pre-operative imaging effect on surgical outcomes	Group 1: Double-positive results ($n = 161$) Group 2: Single-image positive results ($n = 111$) Group 3: Double-negative image results ($n = 39$)	Successful resolution rate after surgical interventions – Group 1: 91.3% (mainly FP or UNE) Group 2: 93.7% (FP or UNE, BNE) Group 3: 89.7% (mainly BNE)
Agirre *et al.* 2022 (59)	Observational study	Impact of preoperative MIBI scan on surgical outcomes	Negative MIBI scans ($n = 120$) Multi-gland disease (14.1%) Peri-thyroid adenoma (69%) Ectopic cervical adenoma (23.9%) Mediastinum adenoma (7.1%)	95% of the patients met the criteria for HPT cure
Caló *et al.* 2013 (14)	Retrospective study	Impact of iOPTH on surgical approach and outcomes in discordant imaging results	Group 1: MIBI and USS positive ($n = 114$) Group 2: MIBI-positive USS-negative ($n = 50$) Group 3: MIBI and USS negative ($n = 11$)	Overall operative success – Group 1: 99.12% Group 2: 98% Group 3: 90.91% In 91% of negative imaging cases, PTH decline was >50% within 10 min
Allendorf *et al.* 2003 (60)	Prospective study	Impact of preoperative MIBI scan on surgical outcomes	Patients with pre-operative MIBI-scan underwent neck exploration – No scan ($n = 137$) Negative scan ($n = 109$) Positive scan ($n = 282$)	The cure rate is higher for both positive and no-scan groups than with negative scans (99.3% vs 92.7%) Shorter operative time for positive scan group than in negative scan group (38.5 (12.6) vs 44.5 (21.9) min)
Harari *et al.* 2009 (61)	Review of medical records	Impact of proper localisation on cure rate	Positive scans ($n = 373$) Negative scans ($n = 44$)	Lower cure rate in patients with negative scans (87.1% vs 96.0%) Longer surgical time (77.3 (52.5) min vs 48.4 (34.6) min) for patients with negative scans
Bergenfelz *et al.* 2011 (22)	Prospective multicentre study	To explore initial surgery outcomes for sporadic PHPT in patients with negative preoperative MIBI scans and USS	Pre-operative negative MIBI and USS (n = 173)	Negative exploration rate for sporadic PHPT – 13.3% Risk of persistent PHPT (After 6 Weeks) – 18%

BNE, bilateral neck exploration; FP, focused parathyroidectomy; HPT, hyperparathyroidism; iOPTH, intraoperative PTH; MIBI, methoxyisobutylisonitrile / 99mTc-Sestamibi; PHPT, primary hyperparathyroidism; PTH, parathyroid hormone; USS, ultrasound scan; UNE, unilateral neck exploration.

for parathyroidectomy. Endocrinologists frequently request MIBI scans, and if the results are negative, patients are less likely to be referred to surgeons, impacting treatment decisions. Surgeons are also influenced by MIBI scans, and if negative, they are less likely to recommend parathyroidectomy. Negative MIBI results were, therefore, independently associated with reduced referrals to surgeons and lower rates of surgery recommendation compared to positive scans, after adjusting for various factors (55). In a retrospective study, a higher proportion of patients with positive scans underwent evaluation by an endocrine surgeon and subsequent parathyroidectomy, whereas those with negative scans had lower rates of assessment and surgery (56). This highlights the importance of referring patients with PHPT to experienced parathyroid surgeons for evaluation, regardless of MIBI scan results.

Potential implications

Understanding patterns in patients with negative MIBI scans, such as single adenomas, enables targeted approaches. Challenges faced by those with discordant localisation, including multi-gland disease, underscore the need for tailored interventions. Strong recommendation for conventional cervicotomy highlights surgical precision. Emphasising iOPTH monitoring suggests its critical role in ensuring successful parathyroidectomy, guiding limited exploration for optimised outcomes. The correlation between weight and oxyphil cell content in positive MIBI scans offers newer insights into PHPT pathophysiology, refining diagnostic and surgical strategies for improved outcomes. Overall, these implications contribute to refining strategies for both diagnosis and surgical interventions, potentially improving patient outcomes and the overall management of PHPT.

Conclusion

This review delves into the complexities of detecting pathological parathyroid glands and focuses on reasons for FN MIBI findings. Factors contributing to scan discordance include smaller lesion size, multi-glandular disease, clear cell dominance, higher fat content, ectopic lesion locations, reduced cellular components within cystic adenomas, lesser mitochondrial counts, lower calcium and parathyroid hormone levels, thyroiditis and thyroid nodular disease, and the presence of the drug metabolism transporter P-gp, thereby subsequently affecting surgeons' decisions and patient outcomes. Discordant imaging can lead to lower cure rates, longer operative times, and delayed referrals, thus advocating for iOPTH monitoring. Future research is needed to refine strategies for diagnosing and managing PHPT.

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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Author contribution statement

BA completed the literature search, collected, assembled the data, and drafted the manuscript. FR edited and critically revised the manuscript. AA finally reviewed and approved the manuscript. All authors consented to the final version of the manuscript.

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