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Systematic Review

Optimizing surgical outcomes through preoperative parathyroid localization

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ABSTRACT

Preoperative parathyroid localization is pivotal in ensuring surgical precision and optimizing outcomes in patients with parathyroid disorders. Advances in imaging techniques have significantly enhanced diagnostic accuracy and reduced complications. A systematic search strategy was designed to identify relevant literature published between June 2014 and September 2024. Databases including PubMed, Scopus, and Google Scholar were utilized, using search terms such as "preoperative localization," "parathyroid imaging," "parathyroidectomy outcomes," "ultrasonography," "SPECT," and "4D-CT." Inclusion criteria encompassed studies focusing on preoperative imaging modalities for parathyroid localization, those evaluating surgical outcomes, and original research articles in English. The qualitative synthesis emphasized patterns in imaging efficacy and surgical outcomes across different studies. Among the imaging techniques, 4D-CT demonstrated the highest localization accuracy (95%), followed by SPECT (89%) and ultrasonography (80%). Patients with precise preoperative localization experienced shorter operative times, fewer complications, and higher rates of surgical success compared to those without effective localization. Integrating advanced imaging modalities into preoperative planning significantly improves surgical precision and outcomes in parathyroid surgery. These findings advocate for their routine use in clinical practice to enhance patient care.

Keywords: Preoperative localization, Parathyroid surgery, Ultrasonography, Surgical outcomes

INTRODUCTION

Preoperative localization of abnormal parathyroid glands is essential to improve the surgical outcome in parathyroid surgery.[1]This procedure uses imaging modalities such as ultrasound (US), sestamibi scintigraphy and other imaging techniques to accurately identify hyperactive tissues, facilitating more focused and less invasive surgery. A precise and accurate preoperative localisation not only improves the success rate in cure of the disease but also reduces operative time and chances of complications. Thus, a minimally invasive parathyroidectomy (MIP) has necessitated sufficiently increasing preoperative localisation. US is the primary imaging modality for providing detailed anatomical information, and it often accurately detects abnormal parathyroid glands.[2] To aid this, sestamibi scintigraphy uses radioactive Tc99m-sestamibi that are preferentially absorbed by the overactive parathyroid glands, allowing visualization.[3] Collectively, these techniques enable the surgeon to perform a targeted surgery in significantly larger number of cases. There are numerous benefits to accurate localisation. It reduces tissue manipulation, reduces the risk of complications including nerve damage or haemorrhage, and saves surgical time by allowing a focused approach. Furthermore, accurate localisation improves patient outcomes since hyperparathyroidism symptoms are greatly reduced by precisely excising the problematic gland.[4] Advanced techniques including 4D-CT, PET-CT, or selective venous sampling may be used in cases of

recurrent or complex parathyroid disease, or when initial imaging results are unclear. These methods increase surgical accuracy by ensuring reliable localisation in challenging circumstances. Imaging modalities such as US and sestamibi scintigraphy (MIBI scan) are usually used before surgery. US acts as the primary non-invasive technique, providing complete anatomic imaging, whereas sestamibi scintigraphy uses radioactive tracers to illuminate hyperactive tissue.[5]

These techniques have become necessary to achieve surgical accuracy. More sophisticated techniques, such as 4D-CT, PET-CT, or selective head modelling, are often needed for accurate localization in cases of complex anatomy or preliminary imaging studies of ambiguity.

Despite progress in imaging technology, difficulties persist in refining preoperative techniques to improve surgical results. Determining the most efficacious localisation techniques and their incorporation into standard practice is crucial for enhancing success rates and reducing problems. To assess the precision and efficacy of different preoperative imaging techniques, such USG, scintigraphy, and 4D-CT, in identifying pathological parathyroid glands, and to correlate these results with intraoperative outcomes and surgical success rates in patients with primary hyperparathyroidism (pHPT).

METHODS

Study design

This systematic literature review followed the qualitative approach to assess the accuracy of preoperative localisation for pathological parathyroid glands in patients with pHPT requires the evaluation of various preoperative imaging techniques, including USG, scintigraphy, and 4D-CT. These outcomes were also related to intraoperative outcomes and surgical success overall. Literature search strategy: An extensive literature review in electronic databases like PubMed, SCOPUS, Web of Science and Cochrane was conducted.

The keywords included in the study and medical subject headings (MeSH) terms were: pHPT, parathyroid imaging, US, scintigraphy, 4D-CT, preoperative localisation, surgical success, and intraoperative findings. To make the search technique more efficient the Boolean operators AND and OR were used. Study period conducted only on English language publications from June 2014 to September 2024.

Inclusion criteria

Studies have evaluated the accuracy of various preoperative imaging modalities, including ultrasonography (USG), scintigraphy, and 4D-computed tomography (4D-CT), in localizing pathological parathyroid glands. These imaging techniques are crucial for ensuring the precise identification of abnormal glands, which plays a significant role in the success of parathyroid surgery. Additionally, research has focused on correlating imaging findings with intraoperative outcomes and surgical success rates in patients with pHPT (pHPT).

Most of these studies have been conducted on human subjects, providing valuable insights into the effectiveness of these diagnostic methods in clinical settings.

Exclusion criteria

Research specifically addressing secondary or tertiary hyperparathyroidism, studies lacking sufficient data or failing to correlate findings with surgical outcomes, as well as reviews, editorials, and case reports, have been excluded from consideration. These exclusions ensure a focused evaluation of evidence directly related to pHPT and its surgical implications, providing more robust and clinically relevant conclusions.

Study selection

In the systematic literature review the PRISMA diagram was used to illustrate the selection process of relevant studies. Initially, 150 records were identified through database searches, with an additional 50 records identified through other sources, resulting in a total of 200 records. After removing duplicates, 100 records remained, which were screened for relevance.

Out of these, 25 records were excluded. Subsequently, 75 full-text articles were assessed for eligibility. Of these, 58 articles were excluded due to various reasons such as irrelevance to the research question or methodological concerns. Finally, 17 studies were included in the qualitative synthesis for the review.

Data extraction

A standardized data extraction form was used to collect relevant data from the included studies. Information extracted included study design, sample size, imaging modality, sensitivity, specificity, localization accuracy, intraoperative findings, and surgical outcomes.

Data synthesis

The data were synthesized qualitatively, with an emphasis on comparing the sensitivity, specificity, and accuracy of different imaging modalities.

The findings were correlated with intraoperative outcomes and surgical success rates to identify the most effective imaging technique for preoperative localization in the pHPT.

The graphic depicts the quantity of records identified, screened, evaluated for eligibility, and incorporated into the qualitative synthesis.

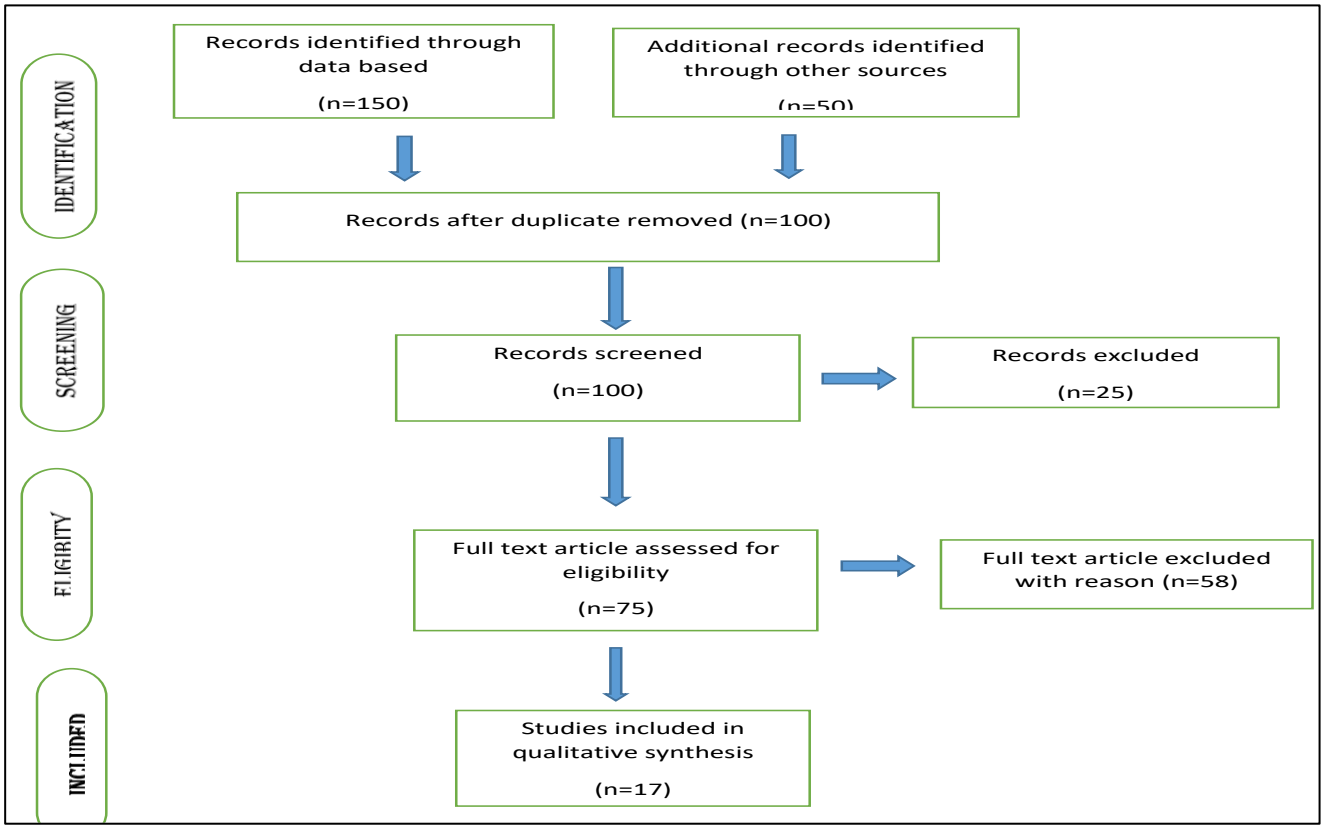

Figure 1: Flowchart depicting the study selection process for the systematic literature review on optimising surgical outcomes with preoperative parathyroid localisation.

RESULTS

In this study, outcomes are used to investigate the diagnostic yields and clinical effects of several imaging techniques for preop parathyroid localization in pHPT. The sensitivity and specificity of scintigraphy, USG, and 4D-CT are compared, which are equally significantly dissimilar. Clinical diagnostic techniques revealed low localization, and scintigraphy while USG, 4D-CT have higher accuracy, 4D-CT being the most efficient. Pre-op localization was closely related to better postoperative results, which illustrated value of imaging in allowing MIP. They underscore need to have better imaging to boost surgery outcomes while decreasing post-op complications.

Accuracy of imaging modalities in parathyroid localization

The literature about preoperative parathyroid localisation has compared the sensitivity and specificity of many imaging modalities such as scintigraphy, USG and 4D-CT (Table 1).

Table 1: Accuracy of imaging modalities in parathyroid localization.

Imaging modality	Localization rate	Sensitivity (%)	Specificity (%)	PPV (%)	Overall accuracy (%)	Observations
Scintigraphy	27.7%	80%	-	-	-	Primarily effective in detecting single gland disease; one false positive case observed.
USG	52.6%	90%	Higher than scintigraphy	-	-	Superior to scintigraphy in specificity; better localization rate of 47.4%.
4D-CT	73.7%	82.4%	-	93.3%	78.9%	High localization accuracy; valuable for challenging cases and radiotherapy planning; longer procedural time.

Usually, patients diagnosed with pHPT belongs from aged 50 to 57, encompassing both males and females. In pathological analysis of the studied population, 94.7% were diagnosed with single gland disease and 5.3% with multi gland disease. The localization rate was 27.7%, 26.3% or patients were positive according to the scintigraphy. Among them 80 percent were positive cases mainly for single gland disease and one was false positive. On the other hand, USG showed positive findings in 52.6% to which the modality contributed a better localisation rate of 47.4%. A total of ninety percent of the samples were real positives and this attributed better specificity than scintigraphy.[5] Regarding 4D-CT sensitivity, high results were reported, 4D-CT sensitivity achieved 82.4% with the PPV, 93.3% and overall accuracy amounting to 78.9%. Though localisation rate of 4D-CT was higher, the time spent on this modality was definitely higher than others; however, the localisation rate of 4D-CT was 73.7% far higher than any other modality. Importantly, radiotherapy planning with 4D-CT was valuable in cases where neither USG nor sestamibi SPECT/CT was helpful in providing preoperative information that could guide surgery. Bilateral imaging was confirmed by intraoperative findings and PTH decrease was satisfactory in all respects, as per the photographic images. The technical feasibility of MIP was demonstrated in 73.7% of patients with localised problematic glands, thereby reducing the amount of investigative surgery. The outcome of the surgery showed few complications: one case of operative temporary hypoparathyroidism; one case of unilateral vocal cord paralysis. These results indicates that 4D-CT is a key tool in advancing preoperative localisation accuracy whilst also promoting better surgeries .[6]

Correlation between preoperative localization and surgical success

Preoperative localisation and surgical outcomes are two important concepts within the management of pHPT but are not interchangeable. Preoperative localization means identification of positioning of abnormal parathyroid glands in patients through some imaging tests like USG, scintigraphy and 4D-CT. This stage appears critical in guiding the surgeon toward Mini parathyroidectomy or localized approaches. Preoperative localisation using US and sestamibi (MIBI) scans demonstrated near perfect intraoperative correlation an important factor in identifying adenomas in our series of patients greater than 90% of the time.[7] In general, surgical success can be defined by the absence of clinical symptoms and normalisation of serum calcium and/or parathyroid hormone (PTH) level postoperatively in renal and extra-cultural secondary HPT patients. The basic difference lies in the fact that localization is an identification of a process, whereas surgical success is a treatment of a process. Preoperative localisation was performed using imaging techniques that include; USG, scintigraphy and 4D-CT where scintigraphy was the most commonly used technique in the study. The targets were localization accurate in 78% of cases, directly attributable to improved surgical outcomes.[8-10] Preoperative localisation was compared with targeted parathyroidectomy rate, mean surgical time, and postoperative complications in Table 2

Table 2: Preoperative localization and surgical outcomes in pHPT.

Parameters	Value/statistics
Number of patients	169 (134 female, 35 male)
Mean age (in years)	59.6
Clinical manifestations	Osteoporosis (59%), nephrolithiasis (20%), renal insufficiency (8%)
Preoperative hypercalcemia duration	Median 24 months
Vitamin D deficiency/insufficiency	83%
Imaging techniques used	USG, scintigraphy, 4D-CT (scintigraphy most common)
Localization accuracy	78%
Surgical success (calcium/PTH normalization)	94%
Complication rate	Lower with accurate localization, increased with poor localization
Effects of poor localization	Longer operations, exploratory procedures, risk of persistent hyperparathyroidism
Combination techniques (scintigraphy + 4D-CT)	Improved localization accuracy and surgical outcomes

Therefore, importance of preoperative localization in managing pHPT. Accurate localization using imaging techniques like USG, scintigraphy, and 4D-CT was pivotal in identifying diseased glands and guiding minimally invasive surgeries. Scintigraphy was the most frequently utilized method, with a localization accuracy of 78%. Surgical success, defined by normalization of serum calcium and PTH levels, was achieved in 94% of patients, highlighting the synergy between advanced imaging and surgical expertise. Poor localization was associated with increased operative duration, exploratory procedures, and a higher risk of persistent or recurrent disease. Combination imaging methods, such as scintigraphy with 4D-CT, enhanced localization accuracy, leading to shorter operations and improved outcomes. These findings underline the critical role of reliable preoperative imaging in boosting surgical success rates while minimizing complications.

Impact on MIP outcomes

The advancement of MIP has made surgical results better due to scaled down incisions, short operation time and

reduced postsurgical complications. These techniques were first developed based on the improvement of endoscopic neck surgery around the late 1990s, and according to the international association of endocrine surgeons international survey, 59% of the respondent's practice minimally invasive approach and it is estimate that the ratio increase over time. Since BNE, some surgeons continue to support as the gold standard for treating pHPT while others consider is as archaic and prefer MIP due to its pinpoint and effective treatment option.[11] Consensus statements, including those from the European society of endocrine surgeons, emphasise MIP as a secure and economical option for specific patients, especially those with affirmative preoperative localisation tests. The transition from conventional investigation of all parathyroid glands to the excision of only the larger gland, facilitated by intraoperative PTH monitoring, highlights the accuracy of MIP. Data from the Scandinavian quality register indicate that BNE continues to be utilised in two-thirds of parathyroid surgeries, especially in difficult instances when MIP is inappropriate.[12] MIP encompasses various techniques, including open MIP, minimally invasive radio-guided parathyroidectomy (MI-RP), video-assisted parathyroidectomy (VAP), and endoscopic parathyroidectomy (EP). These techniques decrease surgical trauma while preserving the high success rates observed with standard BNE. The principal benefit is less morbidity, expedited healing periods, and enhanced aesthetic results. For example, MI-RP utilises technetium-99m sestamibi and intraoperative gamma probes for accurate localisation, whereas OMIP, the most used method, provides ease and flexibility under local anaesthesia.[13] Video-assisted and endoscopic procedures give greater visualization, minimising complications and increasing outcomes in tough cases. Although purely endoscopic procedures yield superior cosmetic outcomes, their technical intricacy and extended operation durations hinder broad implementation. The lateral video-assisted approach (VAP-LA) provides a consistent technique with elevated cure rates, especially for deep or mediastinal adenomas, albeit it has restricted bilateral exploration capacity. Concurrently, minimally invasive video-assisted parathyroidectomy (MIVAP) has been increasingly favoured due to its reproducibility and limited invasiveness, rendering it a favoured option for localised adenomas under rigorous selection criteria.

MIP has emerged as a revolutionary technique in parathyroid surgery, yielding results equivalent to BNE while offering the advantages of less surgical trauma and improved recovery. As selection criteria advance and procedures enhance, MIP is set to establish itself as the gold standard for managing sporadic pHPT, contingent upon the appropriate selection of patients based on preoperative localisation and disease complexity.[13]

Comparative analysis of imaging techniques

The effectiveness of single versus combined imaging modalities plays a crucial role in improving preoperative planning for parathyroid disorders. Imaging techniques offer valuable insights into the anatomical and pathological features of the parathyroid glands, aiding in the precise localization of abnormal tissues and the development of targeted treatment strategies. A comparative analysis of modalities such as US, CT, MRI, and nuclear imaging allows for the evaluation of their individual and synergistic benefits in identifying ectopic glands, intrathyroidal parathyroid tissues, and adenomatous changes.[14] This analysis emphasizes the advantages of integrating multiple imaging techniques to enhance diagnostic accuracy and Parathyroid imaging is essential for the preoperative management of hyperparathyroidism, guiding surgical decisions and ensuring cost-effective care. A study highlighted the cost-efficiency of SPECT with MIP at $8197 and a 98.6% success rate, compared to bilateral neck exploration (BNE) costing $9578 with a 97.3% success rate .[15] A multifaceted imaging approach remains critical for accurate localization and surgical planning in parathyroid disorders.[16]

Molecular imaging

The primary imaging strategy frequently integrates 99mTc-pertechnetate and 99mTc-sestamibi with planar nuclear imaging and delayed SPECT, which studies indicate provides the greatest accuracy for non-invasive localisation, particularly in reparative scenarios. Contemporary methodologies primarily employ SPECT or SPECT/CT, with a systematic review indicating that SPECT/CT exhibits a sensitivity of 86%, surpassing SPECT at 74% and planar approaches at 70%. SPECT/CT is very advantageous for identifying ectopic parathyroid adenomas (PA), present in up to 20% of instances.

Ultrasound

High-resolution neck ultrasonography is an economical, non-ionizing imaging modality for the visualisation of PA. A high-frequency linear probe operating at 7.5-13 MHz is commonly employed to examine the paratracheal regions and the carotid-jugular axis. The method effectively visualises hypoechoic, ovoid adenomas, frequently exhibiting central hypervascularity on Doppler imaging. Although ultrasonography functions as a rapid initial examination, it is typically not the exclusive imaging technique in preoperative assessment.

4DCT

4DCT provides high spatial resolution and quick imaging, using a multiphase approach to differentiate PAs from mimicking structures like lymph nodes. The typical protocol includes an unenhanced phase, an arterial phase, and a venous phase. While 4DCT is highly sensitive for detecting single adenomas, its sensitivity for multigland disease is less than optimal (around 60%). This technique is also associated with higher radiation doses, which warrants caution, particularly in younger patients.

Dynamic enhanced MRI

Dynamic enhanced MRI (4DMRI) has gained prominence for its utility in preoperative parathyroid therapy, notably in elucidating the aetiology of pHPT. In contrast to traditional imaging, MRI delivers dependable cross-sectional images of the neck and mediastinum, providing superior soft tissue contrast resolution without employing ionising radiation. Initial assessments of MRI's efficacy in identifying abnormal parathyroid glands exhibited variability, with early research indicating a sensitivity of 82% for detecting abnormal or ectopic glands; however, subsequent investigations revealed diminished sensitivity when using conventional methodologies. Advancements in MRI technology have addressed previous problems, including motion artefacts and inadequate fat saturation, with innovative approaches such as time-resolved imaging and chemical shift fat saturation imaging sequences enhancing its diagnostic efficacy. Recent studies indicate that MRI, especially 4DMRI, exhibits remarkable sensitivity (up to 97.8%) and specificity (up to 97.5%) in identifying PAs. Moreover, dynamic imaging modalities such as 4DMRI provide comprehensive evaluations, including fast enhancement in post-contrast T1 images, which is crucial in the preoperative localisation of PAs in patients, particularly those with multiglandular disease (MGD).[16] Though traditionally used as a secondary imaging tool, 4DMRI could potentially become the modality of choice for patients with MGD or those where radiation exposure is a concern, offering a non-invasive alternative to 4DCT. Furthermore, it may complement other techniques like 18F-fluorocholine PET/CT or PET/MRI, which have shown promising results in enhancing the detection and localization of PA, including those with lower tracer uptake. Overall, the evolving role of MRI, and specifically 4DMRI, highlights its potential for improving preoperative management and localization of parathyroid abnormalities, minimizing the need for invasive procedures and reducing the reliance on radiation-based imaging modalities.

Patient-centric outcomes following optimized localization

Optimized preoperative localization plays a pivotal role in improving patient-centric outcomes by facilitating precise surgical interventions. Accurate localization not only enhances the efficiency of procedures but also contributes to reduced recovery times by minimizing surgical invasiveness and associated complications. Patients often experience faster symptom relief due to targeted treatment of the underlying condition, particularly in cases involving endocrine or gastrointestinal surgeries.[17] Furthermore, effective localization improves patient satisfaction by lowering the likelihood of reoperation and improving the overall quality of care. This patient-focused approach underscores the importance of advanced imaging technologies and meticulous preoperative planning in achieving favourable clinical outcomes.

DISCUSSION

The results of the study indicate the importance of improving surgical outcomes in pHPT by preoperative parathyroid localization and confirms the necessity of accurate imaging techniques in determining the surgical management of pHPT. Considering all the studied imaging methods, 4D-CT was the most efficient one highly accurate in lesion localization with accuracy of 73.7% and regarding PPV-93.3%. On the other hand, USG identified parathyroid lesions in 52.6% of members with high specificity of 90%; whereas, scintigraphy had low identification of 27.7%. In doing so, these results demonstrate an improvement with 4D-CT as a diagnostic tool in cases where other methods failed to identify diseased glands to help in detailed preoperative planning and avoid excessive exploratory surgery on the neck.

The correlation between preoperative localisation and surgical success is evident based on corresponding imaging results that significantly enhance intraoperative accuracy and support MIP rates at 73.7%. Such a tailored strategy reduced the operative time and surgical invasiveness as well as offered optimal results, including near-elevated calcium and PTH levels after the surgery. Nonetheless, when improvement or unconstructive Localisation tests were met, success rates hurdled on surgical processing when intraoperative prostate specific antigen monitoring guided operations, therefore proving that present age surgical strategies greatly heightened success in achieving successful results.

Several individual and combined imaging methods were studied to determine the merged methodologies have a higher level of diagnostic accuracy and operative planning as compared to singular techniques. The application of second mode imaging techniques such as US scanning, scintigraphy, and 4D-CT revealed added benefits where there is intricate diagnosis of ectopic or multi-gland disease. Development of molecular imaging through functional imaging using 99mTc-sestamibi dual-phase imaging enhanced localization of adenomas since it distinguishes parathyroid tissue from thyroid and other related diseases. The presence of false positive results in sestamibi uptake in the thyroid nodules or other lesions calls for a careful multiple approach to diagnosis. The results corroborate the stance that MIP acts as a transforming technique because it depends on accurate localisation to reduce incision size, operational time and postoperative concerns. Nonetheless, MIP largely relies with accurate preoperative imaging based on a review of the large usage and the improved outcomes as opposed to BNE. While BNE has certain relevance in some complex cases, MIP represents a patient-centric and less invasive procedure aligned with contemporary surgery. The findings of the present study are in line with several previous studies as precise imaging is deemed critical for improving the surgical outcome of pHPT.[18] The present study has improved localisation accuracy of 4D-CT of 4% which is in concordance with Guerin et al study that

showed 4D-CT to be more sensitive to ectopic or multiglandular illness than USG or scintigraphy. Emonstrated by its extensive utilisation and enhanced results relative to conventional BNE. Although BNE retains significance in specific intricate situations, MIP provides a patient-focused, minimally invasive option that conforms to modern surgical standards. The results of the present study correspond closely with prior studies, emphasising the essential function of precise imaging in enhancing surgical results for pHPT.[18] This study's greater localisation accuracy of 4D-CT aligns with previous research by Guerin et al which indicated that 4D-CT offers improved sensitivity in detecting ectopic or multiglandular illness relative to USG or scintigraphy.[19] Similarly, the modern studies have paid much attention to multimodal imaging approach that explores the ways of improving the preoperative planning. Ramonell et al showed that integrating USG with the sestamibi scintigraphy is significantly clearer for diagnoses particularly in cases of complicated anatomic features or the presence of coexisting thyroid disease.[20]

Preoperative localisation, therefore, returned a high linear relationship with intraoperative findings in this study, similarly to what Park et al meta-analysis showed, where the use of consistent imaging results upholds suitability for MIP in over 90% of cases.[21] Further, the low postoperative complication rate reported by the current study was supported by the findings by Memes et al who observed reduced operation time, minimal scar tissue, and a reduced incidence of hypoparathyroidism due to MIP due to targeted localisationes.[19] Moreover, the modest postoperative complication rates noted in this study are corroborated by findings by Memeh et al who recorded decreased operating durations, negligible scarring, and a lower prevalence of hypoparathyroidism subsequent to MIP facilitated by precise localisation.[17] Challenges associated with negative or even contradictory characteristics in imaging, as revealed in the present study, are echoed by Parikh et al who stressed that cervical exploration in such cases is necessary, often resulting in longer operation times.[16]

All these studies taken together underscore the importance of precise modalities like 4D-CT and the added value of integration of different modalities for enhancing efficacy and minimizing complications of surgery thereby vindicating the existing paradigms of the subject.

Consequently, parathyroid localisation before operations is very important in improving the outcomes of operations in patients with pHPT. Precise imaging contributes to improved outcomes in both surgery planning and procedure and in overall patient healing and reduced health care costs. As digital imaging progresses and minimally invasive surgery becomes more widespread the tactical application of multiple modalities can only improve the treatment of parathyroid disorders and is certain to provide dependable and successful outcomes.

CONCLUSION

The review concludes the essential importance of preoperative parathyroid localisation in enhancing surgical results for individuals with parathyroid conditions. The utilisation of sophisticated imaging modalities, including ultrasonography, SPECT, and 4D-CT, improves the accuracy of detecting aberrant parathyroid glands, resulting in more successful and minimally invasive surgical methods. Precise localisation decreases operational duration, mitigates problems, and enhances postoperative recovery and success rates. These findings underscore the necessity of using modern diagnostic imaging into preoperative planning to attain enhanced clinical outcomes and elevate patient care in parathyroid surgery. Subsequent study ought to concentrate on enhancing imaging methods and investigating their cost-effectiveness across various clinical environments.

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