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Impact of combined preoperative ultrasonography and sestamibi scan on surgical planning and patient recovery in primary hyperparathyroidism

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Abstract
Background: Primary hyperparathyroidism (PHPT) is an endocrine condition that is characterized by the overproduction of PTH, which usually needs surgical treatment. Localization of preoperative adenomas is vital to achieve a successful outcome.
Objective: This study aims to determine the effects of preoperative combined ultrasonography and sestamibi scan on surgical planning and postoperative recovery amongst patients of PHPT.
Methodology: The study was a cross-sectional design carried out at Bangabandhu Sheikh Mujib Medical University between July 2022 and June 2023 and included 14 patients with biochemically verified PHPT. Preoperative high-resolution ultrasonography of the neck in all patients and technetium-99 m sestamibi scintigraphy also took place. Focused parathyroidectomy under general anesthesia was done and intraoperative assessments of PTH were carried out before and after excision. Clinical data about demographics, imaging, intraoperative correlation, postoperative complications, length of hospital stay, and cosmetic results were recorded and analyzed using SPSS v22 with the threshold of $p<0.05$.
Result: The mean age of the patients was 32.36±9.76, and 71.4% were males. The most frequent renal symptoms were (64.3%). In 66.6% of left lower and 66.7% of the right lower adenomas, the USG correctly localized the adenomas but failed to detect 28.6% of cases, which were unnoticed and appeared as normal. Localization of lesions with sestamibi scans was 92.9% although there was a 100% concordance of supramediastinal adenomas. Imaging in combination significantly enhanced the capability to localize, reduce excessive dissection. Postoperatively, 57.1% patients experienced bone pain and circumoral paresthesia, 42.9% digital paresthesia, and 14.3% carpopedal spasm, which were all temporary and tolerable. The cosmetic result was very good in all the patients (100%). The reported average duration of hospital stay was 8.2±6.26 days.
Conclusion: The combination of ultrasonography and sestamibi scan added to the surgical accuracy and patient recovery in PHPT, justifying frequent usage as part of preoperative planning.

Keywords: Primary hyperparathyroidism, ultrasonography, sestamibi scan, focused parathyroidectomy, minimally invasive surgery

Introduction
Primary hyperparathyroidism (PHPT) is considered an endocrine disorder that is characterized by excessive parathyroid hormone (PTH) secretion due to an adenoma, resulting in hypercalcemia, skeletal, and renal complications [1]. Surgical management with the removal of the adenoma of the parathyroid gland is the most preferred treatment approach [2], but that needs proper localization. Several imaging studies are available for preoperative localization, including ultrasonography (USG), sestamibi scan, parathyroid four-dimensional computed tomography (4D-CT), parathyroid venous sampling, magnetic resonance imaging (MRI), and positron emission tomography (PET). Neck Ultrasonography (USG) and parathyroid nuclear medicine (Tc-sestamibi) scans are reported as the most standard diagnostic approach for the “roadmap” to the surgeon for a perfect hyperparathyroid surgery, but these imaging techniques can result in false positives or negatives in case of multiglandular parathyroid disease [3]. The prevalence rate of parathyroid hyperthyroidism was 0.84% worldwide from 2007 to 2018 [4]. Another study suggested the global rate of hyperparathyroidism is 1% [5]. A Scottish study claimed that the frequency of primary hyperparathyroidism is increasing to 4.6% for women and 3.2% for men annually in yearly at highly populated countries like Bangladesh [6].

In Bangladesh, patients are also choose parathyroidectomy nowadays [7]. The most common type of operative procedure was usually bilateral neck exploration (BNE), but after discovering lower complication rates, shorter hospital stay, better cosmesis, and similar cure rates, minimally invasive focused parathyroidectomy (MIP) is the new favorite procedure used to treat patients with single gland disease [8]. A combined approach of localizing the affected gland by preoperative Ultrasonography and Sestamibi Scan for Surgical Planning is important for the patient's complete recovery from Primary Hyperparathyroidism. A very few studies in the past were conducted to identify the impact of surgical planning and its success on primary hyperparathyroidism by neck USG and sestamibi. This study aims to evaluate the effect of combined USG and sestamibi scan on preoperative localization and postoperative outcomes in patients treated using focused parathyroidectomy.

Methodology

In the Department of General Surgery at Bangabandhu Sheikh Mujib Medical University, a cross-sectional study was conducted among 14 patients with Primary Hyperparathyroidism (PHPT). The study timeline spanned from July 2022 to June 2023, encompassing participants while adhering to all relevant ethical considerations. Sample collection was done using a convenient sampling process, and the participants were recruited by using their study-specific inclusion and exclusion criteria.

Inclusion criteria

- Patients aged ≥18 years. There is no upper age limit.
- Biochemically diagnosed case of Primary hyperparathyroidism (PHPT).
- Patient with informed written consent.

Exclusion criteria

- Confirmed case of malignancy.
- Double adenomas (DA) or multi-gland disease (MGD) or hyperplasia.
- History of recurrent hyperparathyroidism, thyroid parathyroid adenoma, and ectopic parathyroid adenoma in the mediastinum requiring thoracotomy.
- An associated parathyroid adenoma with other pathology in the neck requires exploration.
- Lack of informed consent.

All patients were subjected to high-resolution neck ultrasonography and Technetium-99m sestamibi scintigraphy 4-6 weeks before surgery. USG was used to evaluate the location and site of enlarged parathyroid glands, whereas sestamibi scans were used to obtain metabolic localization depending on the radiotracer accumulation. The surgical planning was based on the combined interpretation of the two imaging modalities.

Patients were operated under general anesthesia and focused parathyroidectomy done after the optimization of anesthetic and metabolic parameters. Measurement of intraoperative parathyroid hormone (PTH) was done by taking blood sample at pre and post-excision period. The intra-operative identification of the diseased gland compared with pre-operative imaging was conducted.

An individual case report form was created to record patients data. Patients demographic information, imaging report, and post-operative adverse events and recovery timing were collected simultaneously. All data were set to be analyzed on MS Excel and Statistical Package for Social Sciences (SPSS) version 22.0 software. A p-value <0.05 was considered statistically significant in a 95% confidence interval.

Result

The study enrolled 14 patients according to the inclusion and exclusion criteria. All result tables include demographic characteristics, imaging, operational performance, and postoperative outcomes.

Table 1: Distributions of the study patients by demographic profile and presenting and past complaints (N=14)

Variables	Frequency (n)	Percentage (%)
Age (years)		
11-20	3	21.4
21-30	3	21.4
31-40	5	35.6
41-50	3	21.4
Mean± SD	32.36±9.76	
Gender		
Male	10	71.4
Female	4	28.6
Symptoms		
Renal symptoms	9	64.3
Bone symptoms	5	35.7
Abdominal symptoms	5	35.7
Muscle weakness	4	28.6
Fatigue	4	28.6
Memory impairment	3	21.4
History		
Renal disease	5	35.7
Hypertension	3	21.4
Bone disease	3	21.4
Diabetes mellitus	1	7.1
Others	2	14.2

Table 01 interprets this is a male-dominant study with a male-female ratio of 2.5:1. The Majority of the patients were male (71.4%), and a few female participants were noted (28.6%). The mean age was 32.36±9.76 years with an age range of 18-45 years. Renal symptoms were the most frequent presenting complaint (64.3%); each bone and abdominal complaints in 35.7% of patients, respectively. There was also a substantial prevalence (35.7%) of prior renal disease, as an indication of the systemic influence of PHPT.

Table 2: Combined Imaging Findings vs Peroperative Findings (N=14)

Location	USG (%)	Sestamibi (%)	Peroperative (%)
Left lower	-	6 (42.9)	6 (42.9)
Left upper	-	1 (7.1)	1 (7.1)
Right lower	-	4 (28.6)	3 (21.4)
Right upper	-	-	1 (7.1)
Superior mediastinal	-	3 (21.4)	3 (21.4)
Normal	4 (28.6)	-	-

Table 02 shows that Sestamibi has properly located more than 92.9 percent of cases; the USG has failed to identify several lesions, with 28.6 percent being falsely declared to be normal. Combined imaging was significant during surgical planning application that allowed specific operative targeting site and less exploration time.

Table 3: Association between USG of neck with peroperative findings (N=14)

USG of neck	Left lower (n=6)	Left upper (n=1)	Right lower (n=3)	Right upper (n=1)	Superior mediastinal (n=3)	Total (n=14)
Left	4 (66.6%)	-	-	-	-	4 (28.6%)
Right	-	-	2 (66.7%)	1 (100.0%)	1 (33.3%)	4 (28.6%)
Right & Left	1 (16.7%)	-	-	-	-	1 (7.1%)
Right (medial & lateral)	-	-	1 (33.3%)	-	-	1 (7.1%)
Normal	1 (16.7%)	1 (100.0%)	-	-	2 (66.7%)	4 (28.6%)

Table 03 indicates that USG accurately localized 66.6% of left lower adenomas and 66.7% of right lower adenomas. It was precise in right upper adenomas (100%), yet less useful in identifying lesions in the superior mediastinum, as two out of three were missed. Moreover, 28.6% of patients began with normal results on the USG that were obtained even though there were intraoperatively detected abnormal glands.

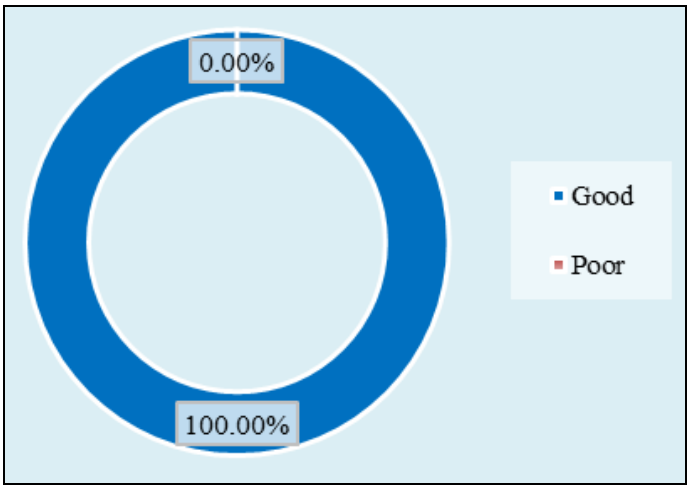

Fig 1: Post-operative cosmetic outcome of patients (N=14)

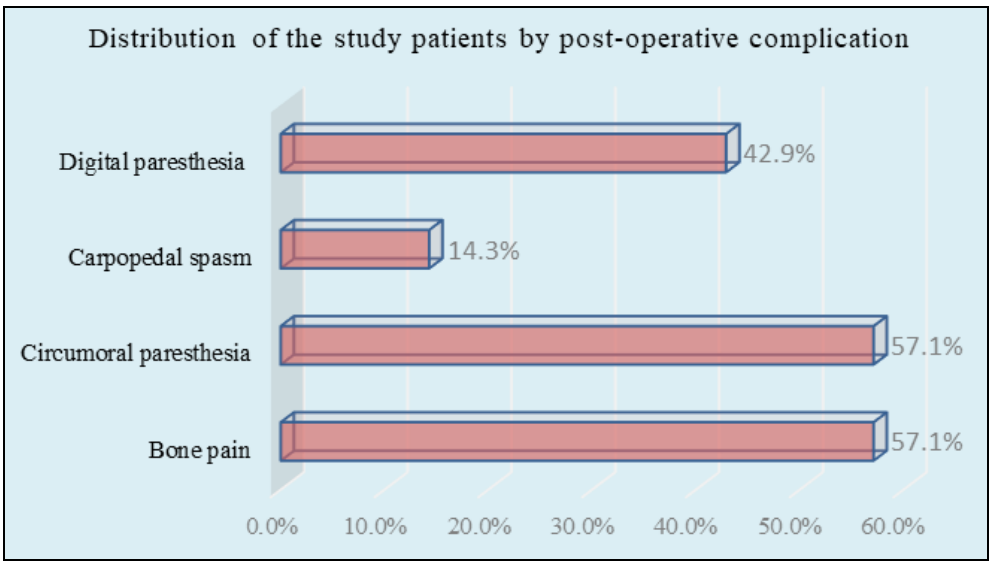

Fig 2: Post-operative complications of patients (n=7)

Table 4: Postoperative Outcomes of Patients (N=14)

Outcome	Frequency (n)	Percentage (%)
Complications (n=7)		
Bone pain	4	57.1
Circumoral paresthesia	4	57.1
Carpopedal spasm	1	14.3
Digital paresthesia	3	42.9
Cosmetic outcome		
Good	14	100
Poor	0	0
Hospital stay (days)	8.2±6.26 (range 2-19)	

Table 04 demonstrates that over 50% of the patients had transient symptoms of hypocalcemia, which included pain in bones and paresthesia. Nevertheless, excellent cosmetic outcomes were achieved by all patients due to the less extensive surgery. Patients with and without complications spent an average of 8.2±6.26 days, respectively, in the hospital.

Discussion

The study combined two widely accepted prediagnostic tools, neck ultrasonography and Sestamibi scan, for surgical planning and to monitor the impact on the patient's recovery from primary hyperparathyroidism. USG and Sestamibi scans benefited as valuable preoperative imaging tools during the second half of the last century. As shown in the studies by Wilhelm *et al.*, 2016; and Varadharajan *et al.*, 2018, several institutions use a mix of ultrasound and Sestamibi scan for preoperative imaging [9, 10]. The results indicated that roughly one third (35.6%) of the patients treated with focused parathyroidectomy were aged between 31 to 40 years, and ages ranged between 18 to 45 years; the average age was 32.36 (SD = 9.76). The analysis established that the majority, 71.4% of the surgically operated patients, were male, and the remaining 28.6% were female. In contrast, a study by Topal *et al.*, 2019 showed that parathyroid diseases requiring surgery were predominantly found in females [11]. In the current study, most hyperparathyroidism patients (64.3%) showed renal manifestations, 35.7% of patients happened to show symptoms around the bones and abdomen, 28.6% of patients showed muscular manifestations and fatigue, and in 21.4% of cases, memory disability had been reported. In the present study, it was identified that the prevalence of renal, bone, and hypertension history was 35.7%, 21.4%, and 7.1%, respectively considered in patients with hyperparathyroidism. Moreover, 7.1% of patients had experienced pancreatitis, and 7.1% had previous chronic calculus cholecystitis. According to previous data, bone mineral density, fractures, bone pain, hungry bone syndrome, gastrointestinal disturbances, neuropsychiatric complaints, nephrocalcinosis, and a higher risk of nephrolithiasis are some associated risk factors of primary hyperparathyroidism [1]. This observation revealed that the accuracy of a USG in locating the exact position of primary hyperparathyroidism was limited. The confinement of adenomas was achieved only in 28.6% of those people who had left or right side USG assessment. This suggests that accurate preoperative localization with a USG by itself is not a possibility. In contrast, the Sestamibi scans were more accurate and revealed 92.9% of patients to be identified. Park HS *et al.*, 2022 quoted that for a successful parathyroidectomy, accurate preoperative localization of parathyroid lesions is essential, and ultrasonography in combination with technetium 99m-sestamibi-single photon emission computed tomography/computed tomography is acceptable in the majority of cases [12]. Nonetheless, the best localization was evident under preoperative evaluations, and in this study, localization was perfect with 100%. The proportion of patients whose sestamibi uptake and intraoperative findings were congruent with the presence of adenomas in the superior mediastinum was also found to be 21.4% in this research. Determination of the precise location of parathyroid adenoma using Sestamibi scans is a very precise procedure, as the concordant scans were dissimilar in all fibers that included left lower, left upper, right lower, right upper, and superior mediastinal scans in 100% of patients. Such a level of accuracy is especially essential as it may lead to less invasive and more focused surgical operations. Khorasani N *et al.*, 2014 performed a similar study using sestamibi scans, and the results ranged between 54.0% and 100.0% concordance of preoperative scans and outcomes at completion of surgery [13]. Simultaneously, the sensitivity of preoperative USG in identifying abnormally large parathyroid glands was very high, particularly in the left lower area and right upper side, where it achieved 66.6% and 100% accuracy, respectively. It also reliably (100.0%) identified correctly displaced parathyroid glands in the right upper position. Its accuracy of 66.7% in the superior mediastinal, as well as the right lower areas, was lower. This combined preoperative localization technique aligns with the findings of several other studies that emphasize the reliability of intraoperative findings in guiding the surgeon to the precise location of the adenoma [14]. Primary Hyperparathyroidism requires a surgical procedure for complete recovery, and in comparison to bilateral neck exploration, focused parathyroidectomy has several benefits, including a quicker recovery time, less surgical dissection, cost savings, a short duration of hospital stay, and a lower risk of temporary postoperative hypocalcemia [15]. In this study, no patient was discharged with an "ugly scar" after surgery. Aesthetic cosmetic outcome rate was successfully 100% for this research. Some post-operative complications were recorded as Bone pain (57.1%), Circumoral paresthesia (57.1%), Carpopedal spasm (14.3%), and Digital paresthesia (42.9%). Murray SE *et al.*, 2013 also found some minor effects like fatigue (98%), muscle aches (89%), bone/joint pain (87%), memory problems (86%), and difficulty concentrating (86%) after parathyroidectomy, which were resolved with time and proper management [16]. The average hospital stay was documented as 8.2±6.26 with a minimum of 2 days post-surgery and a maximum of 19 days. Overall, the study design of merging preoperative Ultrasonography and Sestamibi Scan for surgical planning of primary hyperparathyroidism evident a positive impact on patients recovery. Numerous studies have shown that the combination of sestamibi scans and USG for preoperative localization of parathyroid adenoma produces a diagnostic accuracy of roughly 94.0% to 99.0% which reflects on this study as well [17].

Limitation

The research population was sampled at a single tertiary hospital; therefore, the outcome of the research study may not be the real representation of the country. The current research article is concerned with a very short period. The present study was also limited by too small sample size. Thus, further study with a larger sample size could be undertaken in the future.

Conclusion

Ultrasonography and sestamibi scan can be useful in predicting the site of a parathyroid adenoma in patients with primary hyperparathyroidism, which can aid in adenoma localization. Localization performed preoperatively allows patients to undergo focused parathyroidectomy that has the potential to be cost-effective, decreases the likelihood of postoperative complications, reduces postoperative hospital stay with positive cosmesis and patient satisfaction, and ultimately leads to a superior postoperative outcome.

Abbreviations

- **PHPT:** Primary Hyperparathyroidism
- **PTH:** Parathyroid Hormone
- **USG:** Ultrasonography
- **MIP:** Minimally Invasive Parathyroidectomy
- **BNE:** Bilateral Neck Exploration
- **DA:** Double Adenoma

- **MGD:** Multigland Disease
- **SPSS:** Statistical Package for Social Sciences

Conflicts of Interest

The authors declare no conflicts of interest related to this study.

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