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RESEARCH ARTICLE

Short-term outcomes in post-parathyroidectomy patients at Tygerberg Hospital

R Pargner[1]*, A Coetzee[2], L Martin[1], C Burger[3] and W Conradie[1]

[1]*Department of Surgery, Faculty of Medicine and Health Sciences, Tygerberg Hospital, Stellenbosch University, South Africa*
[2]*Division of Endocrinology, Department of Medicine, Faculty of Medicine and Health Sciences, Tygerberg Hospital, Stellenbosch University, South Africa*
[3]*Department of Medical Imaging and Clinical Oncology, Division of Nuclear Medicine, Faculty of Medicine and Health Sciences, Stellenbosch University and Tygerberg Hospital, Cape Town, South Africa*
Corresponding author, email: r.pargner@gmail.com

Background: Primary hyperparathyroidism (PHPT) often presents asymptomatically but can lead to significant complications. Surgery is the only definitive treatment, with bilateral neck exploration (BNE) and focused parathyroidectomy (FP) both associated with high cure and low complication rates. Limited research exists regarding post-parathyroidectomy outcomes in South Africa (SA).
Objective: This study aimed to describe the short-term outcomes of BNE and FP at Tygerberg Hospital (TBH).
Methods: This retrospective study examined patients who underwent surgery for PHPT between 1 January 2015 and 1 October 2023. Data were extracted from an ethics-approved endocrine surgical database. Surgery type, postoperative complications, i.e. hypocalcaemia, hungry bone syndrome (HBS), recurrent laryngeal nerve (RLN) injury, haematoma requiring surgical intervention, airway complications, surgical site infection (SSI), and seroma and cure rates were investigated.
Results: During the study period, 136 patients underwent surgery for PHTP. BNE was performed in 61 patients and FP in 69, while 6 had a unilateral parathyroid exploration. A cure rate of 91.9% (113/123) was achieved. Hypocalcaemia occurred postoperatively in 31.9% (43/136) of patients, of which 81.4% (35/43) had HBS. One patient suffered a permanent RLN injury, and one patient required re-exploration for a haematoma. No airway obstruction, seroma, or SSIs were reported.
Conclusion: Parathyroidectomy for PHPT at TBH is performed safely and achieves outcomes comparable to international standards. The high incidence of HBS in our setting reflects the severity and prolonged duration of PHPT.

Keywords: calcium, hungry bone syndrome, parathyroidectomy, parathyroid hormone, primary hyperparathyroidism

Introduction

Parathyroidectomy remains the most commonly practised curative treatment option for primary hyperparathyroidism (PHPT), a condition characterised by elevated or inappropriately normal levels of parathyroid hormone (PTH). This invariably leads to hypercalcaemia, which can result in adverse outcomes affecting skeletal, renal, and cardiovascular systems, as well as a range of symptoms often summarised as "moans, stones, groans, and mental overtones". Traditionally, PHPT was treated via bilateral neck exploration (BNE); however, advancements in preoperative localisation techniques have facilitated less invasive approaches, such as focused parathyroidectomy (FP). BNE and FP are well established as effective surgical treatment options, with international studies demonstrating high success rates and minimal complications.[1]

The incidence of PHPT ranges from 0.7% in the general population to 3% in postmenopausal women.[1] Research on PHPT in South Africa (SA) is limited. A study conducted at Groote Schuur Hospital in 1987 reported hypercalcaemia in 0.08% of inpatients, with PHPT accounting for 16.5% of cases.[2] The most common cause of PHPT is a single adenoma (84%), followed by multiple gland hyperplasia (15%), with multiple adenomas and parathyroid carcinoma being rare (1%).[3] PHPT is also associated with MEN1 and MEN2a syndromes, necessitating careful evaluation in these patients. Surgical removal of the affected gland remains the only curative option.

The American Association of Endocrine Surgeons (AAES) recommends parathyroidectomy for all symptomatic patients, those aged 50 years or younger, and individuals with a serum calcium level of more than 1 mg/dl or 0.25 mmol/l above the upper limit of normal, also suggesting consideration in asymptomatic patients.[4] Furthermore, the guidelines for the treatment of asymptomatic PHPT of the fourth international workshop recommend surgery in patients with evidence of skeletal and renal end-organ involvement.[5]

Different anatomical and functional localisation studies can be performed to identify the pathological glands. These include ultrasound (US), parathyroid scintigraphy, and 4-dimensional computed tomography (4D CT) scan. In a study by Yeh et al.,[6] the overall sensitivity for patients with PHPT was 58% for a dual-phase ^{99m}Tc Sestamibi SPECT/CT and 79% for 4D CT with a specificity of 99% and 96%, respectively.[6] Woods et al.[7] demonstrated a sensitivity of 95% and specificity of 89% for dual tracer subtraction SPECT-CT, a method also used at our facility.[7.]

Over the years, parathyroidectomy has become safer, with better long-term outcomes and fewer complications. Abdulla et al.[8] confirm better long-term results in hospitals performing higher volumes of parathyroidectomy.[8] BNE requires a 3–4 cm incision, allowing inspection of all four glands, and is suitable for patients with non-localised disease and when suspecting

multiple-gland disease in cases such as MEN1 and 2a, familial PHPT, and lithium-induced PHPT. In contrast, FP allows a smaller 2 cm incision, focusing on the localised pathological gland, and can be performed as an outpatient procedure under general or local anaesthesia. Intraoperative PTH (IOPTH) can improve the likelihood of cure in FP, guided by the Miami criteria, where an IOPTH decreasing by 50% or more after 15–20 minutes predicts cure.[9] More recently, Udelsman et al. developed a curve-based prediction model to predict cure more accurately, measuring PTH levels at different time points intra- and postoperatively and calculating the likelihood of cure from this data.[10]

International studies indicate comparable long-term outcomes for both surgical approaches. In a randomised control trial conducted by Westerdahl and Bergenfelz, FP with IOPTH monitoring provided the same long-term results as BNE.[11] Udelsman et al.[12] reported a 99.4% cure rate and 1.45% complication rate for FP, compared with 97.1% and 3.1% for BNE.[12] In this study, IOPTH monitoring was performed to ensure a sufficient drop in PTH. Recurrent laryngeal nerve (RLN) injury occurred in less than 1% of patients in both groups. A meta-analysis by Singh Ospina et al.[13] confirmed similar cure and complication rates, with postoperative hypocalcaemia occurring in 14% of BNE and 2.3% of FP cases. Infection and mortality rates were also comparable (0.5% and 0.5% for BNE vs. 0.1% and 0.5% for FP).

Data on parathyroidectomy outcomes in SA are limited. A case series of 15 patients with PHPT undergoing FP at Chris Hani Baragwanath Hospital between January 2013 and December 2014 demonstrated a strong correlation between preoperative imaging, intraoperative findings, and postoperative results. FP in this series achieved a 100% cure rate, with only one case of hypocalcaemia and one instance of temporary RLN palsy.[14] A recent audit conducted at the University of the Witwatersrand of 252 patients with PHPT, including 113 who underwent FP, noted higher rates of persistent hypercalcemia in patients with multiple-gland disease of 59.3% (16/27) compared with single-gland disease 9.6% (15/157). Outcomes associated with BNE and FP were, however, not studied.[15]

This study aimed to describe the short-term outcomes of BNE and FP at TBH.

Methods

Study design and setting

This retrospective descriptive study was conducted at TBH, Cape Town, SA. Patients undergoing parathyroid surgery for PHPT between 1 January 2015 and 1 October 2023 were included, and secondary and tertiary hyperparathyroidism and parathyroid carcinoma were excluded.

Ethics

The research complied with the World Medical Association Declaration of Helsinki ethical principles for medical research involving human subjects. It was approved by the Stellenbosch University Health Research and Ethics Committee (Project ID 9526, Ethics Reference Number N19/04/051) and local hospital authorities. Based on the retrospective nature, fully anonymised data, and standard practice assessment, the ethics committee waived the need for informed consent.

Data collection

Data were captured and managed using REDCap (Research Electronic Data Capture; https://project-redcap.org/) hosted at Stellenbosch University. REDCap is a secure, web-based software platform designed to support data capture for research studies, providing (i) an intuitive interface for validated data capture; (ii) audit trails for tracking data manipulation and export procedures; (ii) automated export procedures for seamless data downloads to standard statistical packages; and (iv) procedures for data integration and interoperability with external sources.[16.]

Study variables

The captured variables included demographics (age, sex), symptomatology, biochemical profiles, indications for surgery, localisation, operative details, and post-surgical outcomes. Indications for surgery were defined as age < 50 years, serum calcium > 2.75 mmol/l, decreased bone mineral density (BMD) or vertebral fractures on dual-energy X-ray absorptiometry (DEXA) scan, renal complications such as renal calculi and impairment of renal function, or symptomatic patients. The BMD World Health Organization (WHO) definition for osteoporosis (T-score below −2.5) and osteopenia (T-score between −1 and −2.5) were used. Captured confounders of osteoporosis included smoking, steroid use, and concomitant rheumatological disease (systemic lupus/rheumatoid arthritis). Renal dysfunction was defined as an abnormal creatinine level (females > 90 µmol/l, males > 104 µmol/l). Complications included hypocalcaemia, hungry bone syndrome (HBS), RLN injury, haematoma requiring surgical intervention, airway obstruction, seroma, and surgical site infection (SSI). Hypocalcaemia was defined as a serum calcium level < 2.14 mmol/l after the third postoperative day, and HBS was defined as persistent severe hypocalcaemia below 1.9 mmol/l after day 3, requiring supplementation. While a rapid drop of IOPTH perioperatively is described as a predicting factor for postoperative hypocalcaemia in the literature, this was not consistently available in our study group and therefore was not included.[17] A biochemical cure was defined as a calcium level below 2.55 mmol/l at 6 months or patients with hypercalcaemia due to another cause and suppressed PTH. Note that PTH was not consistently measured postoperatively and was therefore not included to define cure.

Biochemistry

All biochemical analyses were performed at the National Health Laboratory System (NHLS), an SA National Accreditation System (SANAS) accredited laboratory at TBH. NHLS laboratories are accredited by SANAS for compliance with international standards (ISO 15189:2007). Biochemical markers investigated were preoperative serum PTH (normal range 1.6–6.9 pmol/l), pre-, peri – and postoperative serum calcium (2.14–2.50 mmol/l), preoperative serum phosphate (0.78–1.42 mmol/l), serum urea (2.1–7.1 nmol/l), creatinine (females 49–90 µmol/l, males 64–104 µmol/l), alkaline phosphatase (42–98 IU) and Vitamin D levels in nmol/l before supplementation. Serum calcium levels were analysed with a Roche Cobas® analyser (Roche Diagnostics, Basel, Switzerland) through spectrophotometric detection and serum PTH and Vitamin D via electrochemiluminescence binding assay. The NHLS reports Vitamin D levels as sufficient, insufficient, and deficient. However, the ranges provided vary. One reference system defines deficient as < 50 nmol/l, insufficient as 52.5–72.5 nmol/l, and sufficient > 75 nmol/l. The other definition is deficient < 30 nmol/l, insufficient as 30–50 mmol/l, and sufficient >

50 mmol/l. The categorisation was made depending on the reference range provided by NHLS.

Localisation

Pathological glands were localised using one or multiple imaging modalities: US performed by the radiologist on duty that day, surgeon-operated US performed by the attending surgeon at the endocrine surgery clinic, parathyroid scintigraphy, or a 4D CT scan. The dual tracer subtraction method is used at our institution for scintigraphy. While it is routine practice at our unit to perform an US at the patient's clinic visit and again intraoperatively, this was not consistently documented. Therefore, only available records were utilised. 4D CT scan is used as second-line imaging in our unit, with indications being discordant parathyroid scintigraphy and US, prior neck surgery, ectopic location, or concomitant multinodular goitre.

Statistical analysis

A sample size calculation was not performed for this study due to its retrospective nature, which involved analysing pre-existing data from all eligible patients within the specified timeframe. Data analysis was performed using IBM SPSS Statistics version 29 (IBM Corp, Armonk, NY, USA). Descriptive statistics such as counts, proportions, 95% confidence intervals, means and standard deviations, median, and interquartile ranges were used to summarise cure rates, outcomes, and complications. Comparative analysis with international studies was conducted descriptively.

Results

A total of 183 patients underwent parathyroidectomy at TBH during the study period (Figure 1). Forty-seven patients with secondary and tertiary hyperparathyroidism were excluded, resulting in a study population of 136. Twelve patients were lost to follow-up and thus excluded from the cure-rate calculation, as well as one patient with parathyroid carcinoma. The median age of the study population was 61 years, with the majority (80.9%; 110/136) being female. Symptoms were present in half the population (50%; 68/136). Factors contributing to osteoporosis, such as smoking, steroid use, and rheumatological disease, were present in less than 25% of the population. A DEXA scan was available for 113 patients (83.1%), of which 61.9% (70/113) were abnormal. Osteopenia was found in 28.8% (32/113), and 34.2% (38/113) had osteoporosis based on spine, hip, and femoral head measurements or a prevalent vertebral fracture. Most patients had two or more indications for surgery. Table 1 provides an overview of patient characteristics.

Serum calcium levels were monitored six hourly postoperatively and for three consecutive days to screen for hypocalcaemia and HBS. Postoperative serum calcium levels gradually decreased as expected from a median level of 2.83 mmol/l (IQR 1.91) at index presentation to 2.23 mmol/l (IQR 1.62) after day 3. The median perioperative calcium levels with the respective ranges and the PTH level at presentation are indicated in Table 2.

Localisation

As the gold standard imaging modality, parathyroid scintigraphy was performed in 94.1% (128/136) of patients, localising most commonly to the right inferior (28/128, 22.7%) and left inferior (26/128, 20.3%) parathyroid glands. US was performed in 56.6% (77/136) of patients and in 40% (31/77) of these patients the sonographer was unable to identify any parathyroid glands, with 12% (9/77) reported as indeterminate. The most commonly localised pathological glands on formal US were left inferior (13.0%, 10/77), right inferior, and left superior parathyroid glands, each accounting for 10.4% (8/77). Although routine surgeon-performed US is practised in our unit, this was not well documented and in only 44 (32.4%) cases were these results captured. With this modality, pathological gland localisation was achieved in 86.4% of the patients, with the most common sites being the left inferior (13/44, 29.5%) and the right inferior (12/44, 27.3%) parathyroid gland. 4D CT was performed in 36 patients (26.5%). Of those, the most commonly localised parathyroid glands were right inferior (9/34, 26.5%) followed by ectopic (7/34, 20.6%), and multiple glands (4/34, 11.8%). In 17.6% (6/34) of 4D CT scans, no parathyroid glands could be localised.

Surgery

Of the 136 patients undergoing surgery for PHPT, 69 had FP, 61 had BNE, and 6 had unilateral neck exploration. In the BNE group 28 patients, or 20.6% of all patients, had more than one parathyroid gland removed. Three patients had a removal

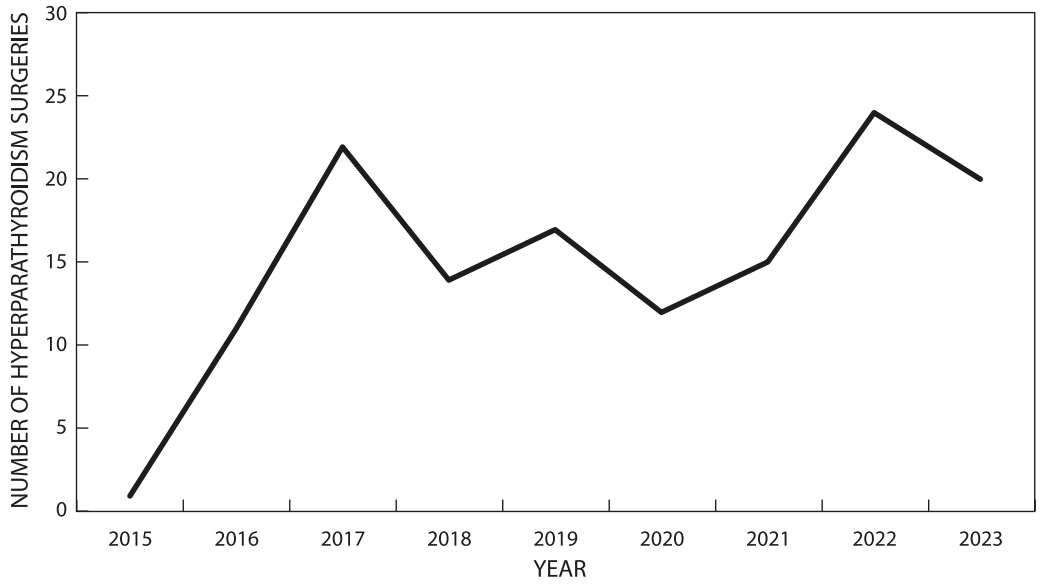

Figure 1: Number of surgeries over the study years.

Table 1: Clinical characteristics and biochemistry of patients operated on for primary hyperparathyroidism

Clinical characteristics	No. (%)
Female	110 (80.9%)
Male	26 (19.1%)
Other comorbidities and risk factors for bone involvement	
Hypertension	82 (60.3%)
Smoker	24 (17.6%)
Steroid use	3 (2.2%)
Rheumatological disease	6 (4.4%)
Indications for parathyroidectomy	
Age < 50 years	27 (19.9%)
Calcium > 2.75 mmol/l	101 (93,4%)
Decreased BMD	70 (61.9%)
Renal complications	35 (25.7%)
Symptomatic	68 (50%)
Number of indications for surgery	
One	27 (19.6%)
Two	52 (38.2%)
Three	44 (32.4%)
Four	12 (8.8%)
Five	1 (0.7%)
Biochemical parameters	
Total serum calcium in mmol/l	
Ca 2.20–2.50	2 (1.5%)
Ca 2.51–2.74 mmol/l	33 (24.6%)
Ca 2.75–2.99 mmol/l	66 (48.5%)
Ca 3.00–3.49 mmol/l	26 (19.1%)
Ca >3.49 mmol/l	9 (6.6%)
Phosphate < 0.78 mmol/l	37 (27.2%)
Vitamin D	
Sufficient	29 (21.3%)
Insufficient	45 (33.1%)
Deficient	55 (40.4%)
ALP > 98 IU/dl	63 (46.4%)
Elevated serum creatinine (F > 90 µmol/L, M > 104 µmol/L)	38 (27.9%)

F = female; M = male.

of an ectopic parathyroid gland, one through BNE and two through FP (Figure 2).

Intraoperative nerve monitoring was utilised in 53 patients (40.0%). Two patients required reoperation to remove a further pathological parathyroid gland; however, those operations were not included in the cure analysis (Figure 3).

The most common diagnosis confirmed on histology was parathyroid adenoma (111 patients, 81.0%). Parathyroid hyperplasia was found in 16 patients (12.0%), and six patients (4.4%) had normal parathyroid tissue in their histology sample. One patient was diagnosed with parathyroid carcinoma, and one with a parathyroid cyst without any features of malignancy.

Postoperative calcium levels dropped in the early postoperative phase and stabilised long-term (Table 3, Figure 4)

Postoperative hypocalcaemia occurred in 43 patients (31.8%). HBS was the most common complication and occurred in 35 patients (25.7%, representing 90% of patients with postoperative hypocalcaemia). One patient had concomitant thyroid pathology and thyroidectomy, which was complicated by permanent RLN injury, and one patient required re-exploration for a haematoma. There were no instances of airway obstruction, seroma, or SSI in the studied population.

Cure after parathyroidectomy was achieved in 113/123 (91.9%). Ten patients (8.1%) were noted to have persistent disease, of which two underwent reoperation (Table 4).

Discussion

This study describes the short-term outcomes of parathyroidectomy in PHPT in 136 patients at TBH, a tertiary referral centre. The definition of a high-volume centre varies throughout the literature but is commonly considered more than 20–40 surgeries per year.[18–20] Since 2015, the number of parathyroid surgeries at TBH has fluctuated and subsequently, from 2022, over 20 surgeries are performed annually with an increasing trend. TBH serves a population of 3.4 million people and is the only centre within this population performing parathyroid surgery. Yeh et al.[21] reported the incidence of PHPT to be 65.5/100,000 in women and 24.7/100,000 in an ethnically diverse population.[21] Therefore, it suggested that PHPT is underdiagnosed in our setting, most likely due to limited access to health care. This is further supported by the advanced stages of disease that patients presented with. Awareness of hyperparathyroidism should be raised amongst clinicians and patients.

Most of our patients were female and above the age of 50, which ties into the patient profile described in international literature.[22,23] More than half of the cohort were hypertensive and most patients had insufficient or deficient Vitamin D levels, both described as risk factors for PHPT.[24,25] Seventy-four per cent of patients had a severely elevated serum calcium level above 2.75 mmol/l, but 50% did not display any clinical symptoms. Asymptomatic PHPT is a well-known problem, as undetected disease can lead to severe complications. For instance, 62% of our patient population had a decrease in BMD on the Dexa scan. Increased bone metabolism was shown with increased serum ALP in 46% of patients and evidence of hypophosphataemia in 27%. Studies have concluded that BMD decreases over time even in asymptomatic patients or patients with mild PHPT, if not treated surgically.[26–28] Renal complications such as nephrocalcinosis and renal impairment were common in the 1970s but have decreased over the decades to 10–20% of

Table 2: Median serum calcium and PTH levels and ranges at presentation and during the perioperative period

Item	Presentation	Admission	6 h	12 h	18 h	Day 1	Day 2	Day 3	> 3 days
Ca in mmol/l (IQR)	2.83 (1.91)	2.76 (1.15)	2.5 (1.64)	2.42 (1.16)	2.36 (1.70)	2.30 (1.59)	2.25 (0.84)	2.22 (1.07)	2.23 (1.62)
PTH in pmol/l (IQR)	16.8 (205.9)								

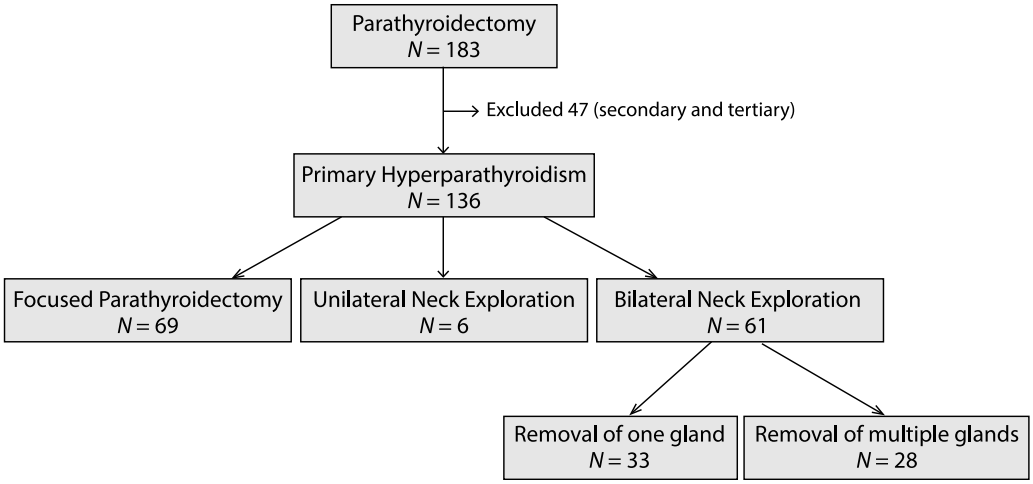

Figure 2: Types of operations performed for PHPT.

patients with PHPT.[29] However, it was more frequently detected in our patients, indicating once again that patients present with more advanced disease in our setting. This is further substantiated by the majority (80%) of our patient population having two or more indications for surgery. Routine investigation of PTH levels in patients with hypercalcaemia or evidence of decreased BMD at primary contact may lead to earlier diagnosis and detect PHPT in patients who might otherwise remain undiagnosed. While age > 50, serum calcium > 2.75 mmol/l, decreased BMD, renal complications, and symptomatic disease were shown to be valid indications for surgery, our study further solidifies that surgery should be considered even in asymptomatic patients who do not fulfil the above criteria.

Localisation of pathological parathyroid glands is a common challenge in the workup of patients with PHPT, potentially necessitating a more extensive procedure and posing a risk for persistent disease post-surgery. Furthermore, there is a discrepancy between localisation on parathyroid scintigraphy and 4D CT and the location of surgically removed pathological glands in our study. Note that 4D CT was only performed as second-line imaging in 36 patients with previous negative localisation or complicated cases. Yeh et al.[6] report a sensitivity of 79% for 4D CT and 58% for dual phase 99m-Tc Sestamibi SPECT/CT, which improved to 81% when both modalities were combined.[6] Specificity was 96% for 4D CT and 99% for dual-phase scintigraphy. In a study on effective factors for the sensitivity of 99m-Tc MIBI scintigraphy, Khorasani and Mohammadi[30] reported a sensitivity of 70%, with the pickup rate decreasing significantly with lower PTH levels.[30] While the dual tracer subtraction method, also used at TBH, has been shown to have a higher sensitivity, it still has a lower sensitivity in multi-gland disease compared with single-gland disease. Nichols et al.[31] demonstrated a sensitivity of 61% for multi-gland disease vs. 97% for single-gland disease using dual tracer scintigraphy.[31] F-18 Fluorocholine PET/CT's localisation performance in PHPT has been assessed more recently. Seyedinia et al.[32] showed a sensitivity between 93% and 99% with a specificity of 75% to 91%, depending on the severity of disease.[32]

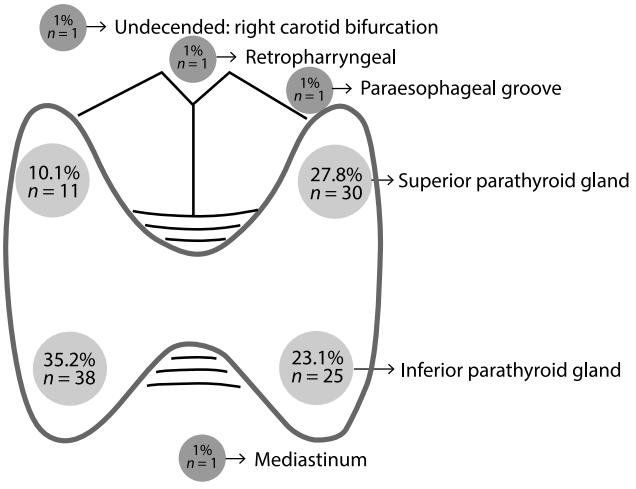

Figure 3: Number and location of pathological single glands removed

In a recent meta-analysis and systematic review by Quak et al.,[33] F-18 Fluorocholine PET/CT showed a pooled patient-based sensitivity of 93.8% with a cure rate of PET-guided surgery of 92.8%.[33] When compared with 99m-TC Sestamibi scan, F-18 Fluorocholine PET/CT had a higher sensitivity of 97% vs. 55% for Sestamibi in a sub-analysis of a study by Whitman et al.[34] F-18 Fluorocholine PET/CT appears to outperform parathyroid scintigraphy with SPECT and 4D CT, particularly in specificity. It could be a promising option, especially in patients with unsuccessful previous localisation and multi-gland disease. This modality is, however, currently not available in SA.

The number of FP and BNE performed was nearly equal. This is in part due to the presence of multi-gland disease in 28 patients and inconclusive preoperative localisation or the presence of ectopic glands. Both approaches performed well with minimal intra- and postoperative complications related to the procedure. Unsuccessful preoperative localisation necessitated unilateral exploration in six patients, again underlining the importance of implementing a better approach to difficult localisation.

The inferior parathyroid glands were more commonly affected than the superior parathyroid glands, with the right inferior parathyroid gland being the pathological gland that was most frequently affected. A study by LoPinto et al.[35] on 810 patients with single-gland disease showed similar results regarding pathological parathyroid gland location.[35] Pathological parathyroid glands were predominantly the inferior glands (68.6%) than the superior glands (31.5%), and in men, the right inferior

Table 3: Number and percentage of patients with normo-, hyper-, and hypocalcaemia over time

Item	Day 1 (*n* = 128)	Day 2 (*n* = 92)	Day 3 (*n* = 81)	> Day 3 (*n* = 109)	3 months (*n* = 107)	6 months (*n* = 86)	1 year (*n* = 95)
Normo- calcaemia	87 (68.0%)	55 (55.6%)	47 (57.0%)	63 (57.4%)	77 (73.3%)	67 (77.9%)	69 (72.6%)
Hyper- calcaemia	18 (14.1%)	11 (11.1%)	10 (12.7%)	7 (6.4%)	18 (17.1%)	15 (17.4%)	19 (20%)
Hypo- calcaemia	23 (18.0%)	33 (33.3%)	24 (29.6%)	39 (35.8%)	10 (9.5%)	4 (4.7%)	7 (7.4%)

gland was the most common location.[35] LoPinto et al. further point out that the inability to successfully localise the pathological parathyroid gland on imaging is a commonly encountered problem during a patient's workup.[35]

Interestingly, in the BNE group, the parathyroid glands most frequently removed were left superior, followed by right and left inferior, and, lastly, right superior. One patient in this group had normal parathyroid tissue on histology, and one had removal of an ectopic parathyroid gland. The above suggests that in cases where preoperative localisation of the pathological parathyroid gland proves challenging, exploration could start with the inferior glands and, more specifically, the right inferior gland.

While our complication rate was low, one patient had a permanent RLN injury. This patient required a thyroid lobectomy for a thyroid mass, and the RLN needed to be shaved off the thyroid. The permanent RLN damage, in this case, was an unavoidable and expected complication. Hypocalcaemia is a well-recognised and common occurrence following parathyroidectomy in patients with PHPT, resulting from multiple factors. The abrupt drop in PTH levels postoperatively leads to a temporary decrease in serum calcium. While some patients may experience below-normal calcium levels, this is a natural consequence of the surgery rather than a complication. Several risk factors for postoperative hypocalcaemia have been identified.

Mittendorf et al.[36] investigated the incidence of hypocalcaemia in 166 patients who underwent parathyroidectomy for primary or secondary hyperparathyroidism.[36] In this study, 42% of all patients with PHPT developed postoperative hypocalcaemia compared with 35.8% in our study population. Subtotal parathyroidectomy was a risk factor for postoperative hypocalcaemia. Only one patient in our study group had a subtotal parathyroidectomy and this patient developed profound hypocalcaemia requiring supplementation. One of the main contributors to postoperative hypocalcaemia is preoperative Vitamin D deficiency, which impairs intestinal calcium absorption. Notably, the 39 patients with biochemical hypocalcaemia beyond the third postoperative day had low Vitamin D levels at presentation. Although they received supplementation, Vitamin D levels were not consistently monitored after surgery.

Westerdahl and Bergenfelz[11] identified the type of neck surgery (FP vs. BNE) as an independent risk factor for early hypocalcaemia with BNE, or the removal of multiple glands posing a higher risk than FP or the removal of single glands.[11] In our study, 25.7% (35/136) patients developed HBS, a condition marked by postoperative rapid bone remineralisation, which contributed to the high incidence of transient hypocalcaemia. Type of neck surgery or single vs. multi-gland disease did not seem to affect the development of HBS. This appears instead to be brought on by the severity and long duration of PHPT in our study population. In the majority of patients, calcium levels stabilised long-term. The incidence of persistent hypocalcaemia was low and could be managed with supplementation. Of the seven patients with significant hypercalcaemia at three months, serum calcium levels normalised or dropped below 2.75 mmol/l in all but two cases, which involved persistent disease.

Our study showed an overall cure rate of 91.9%, with a low complication rate and persistent disease in 8.1% of patients. While this is slightly lower than the cure rate of 98% for BNE and 97% for FP, as reported in the study by Singh Ospina et al.,[13] it is still an acceptable result. A Cochrane review by Pappachan et al.[37] reported on eight trials in which a cure rate of 98% in three and 100% in five studies was achieved.[37] Note that

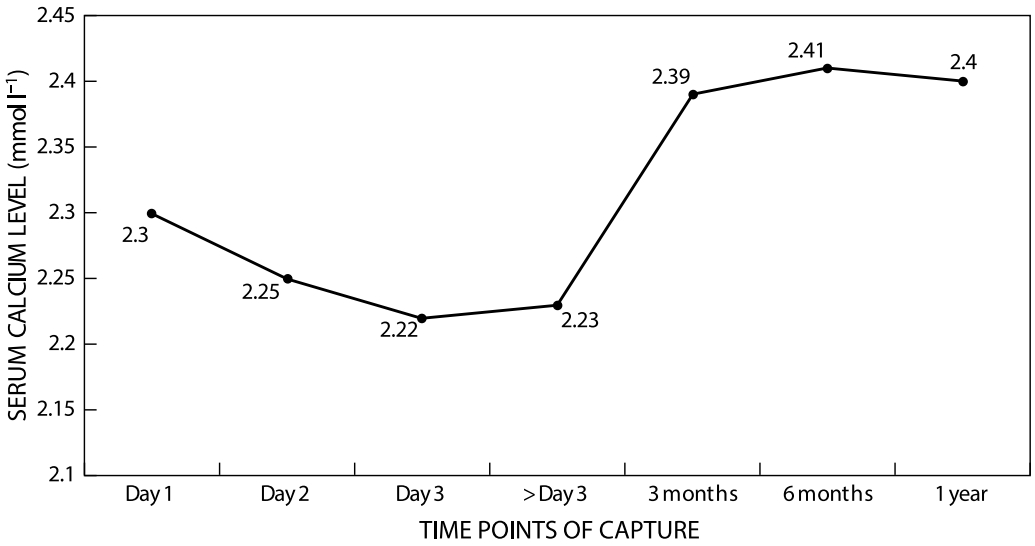

Figure 4: Median serum calcium level in the postoperative phase. X axis: time points of capture, Y axis: serum calcium level in mmol/l.

Table 4: Pre-, intra-, and postoperative findings in patients with persistent disease

Patient	Preop	Operation	IOPTH	Frozen section	Follow up	Relocalisation	Reoperation	Final Outcome
1	PTH 13.2 Ca 2.8	FP R inf intrathymic	0 mins: 4.9 10 mins: 4.9 20 mins: 2.8	Yes	PTH 10.9 Ca 2.54	No	No	Persistent disease (normo-calcaemic)
2	PTH 9.4 Ca 2.59	BNE R inf Other normal	No	Yes	PTH 5.9 Ca 2.64	No	No	Persistent disease
3	PTH 42.9 Ca 3.0	UE L sup L inf normal	No	Yes	PTH 50.0 Ca 2.94	4D CT scan retropha-ryngeal	Yes	Cure
4	PTH 7.3 Ca 2.96	BNE L inf and sup	0 mins: 22 10 mins: 4.03 20 mins: 3.36	Yes	PTH 8.8 Ca 2.71	No	No	Persistent disease
5	PTH 16.1 Ca 2.96	BNE R inf and sup	No	Yes	PTH 13.3 Ca 2.54	No	No	Persistent disease (normo-calcaemic)
6	PTH 13.3 Ca 2.68	BNE Multiple Lns	No	No (lymph node)	PTH 12.6 Ca 2.57	No	No	Persistent disease
7	PTH 38.3 Ca 2.74	UE L sup	0 mins: 20.7 10 mins: 8.1 20 mins: 6.1	Yes	PTH 9.2 Ca 2.79	4D CT mediastinal	Yes	Cure
8	PTH 31.3 Ca 2.73	UE R thyroidec-tomy	No	Yes (intra-thyroidal)	PTH 31.7 Ca 2.70	4D CT mediastinal	No, but planned	Persistent disease
9	PTH 16.8 Ca 2.74	FP L inf	No	No (lymph nodes)	Not available	No	No, but planned	Persistent disease (treat breast ca)
10	PTH 12.2 Ca 2.85	TT and CLND: L inf	No	Yes	PTH 21.0 Ca 2.69	No	No, but planned	Persistent disease (treat thyroid ca)

R = right; L = left; FP = focused parathyroidectomy; BNE = bilateral neck exploration; UE = unilateral exploration; Inf = inferior; Sup = superior; Ln = lymph nodes; 4D CT = four-dimensional computed tomography scan; TT = total thyroidectomy; CLND = central lymph node dissection; ca = cancer; reference range PTH 1.6–6.9 pmol/l, serum calcium 2.14–2.50 mmol/l.

timeous IOPTH monitoring, standard practice in most centres worldwide, is unavailable in our setting. While IOPTH levels are performed in some patients, these are sent to the laboratory and only become available after an hour or more.

In the three persistent cases where IOPTH was used, they fulfilled the Miami criteria and predicted a cure but still had persistent disease, which was falsely reassuring. Future studies on using IOPTH in our population can be of value.

It is worthwhile examining the 10 patients with persistent disease more closely to determine whether, based on preoperative assessments and intraoperative findings, persistent disease was likely or could have been avoided. In most cases of persistent disease, localisation was either inconclusive, failed to identify multi-gland disease, or localised to a normal gland. Only two patients required reoperation, carried out shortly after the index surgery, and both achieved cure. In the remaining eight patients, one underwent further localisation studies, which failed to identify another pathological parathyroid gland. All eight patients were clinically followed up and did not undergo reoperation.

Limitations

The most significant limitation of this study was missing data. Of the 123 patients in the outcome analysis, only 86 had serum calcium taken at 6 months and 95 at one year. Although surgeon-operated preoperative US is part of our unit's standard workup, only 44 reports were available. Documentation of intravenous or oral calcium supplementation, Vitamin D supplementation, and preoperative administration of bisphosphonate need to be more consistent. IOPTH is standard practice in many international units; however, the cost is prohibitive in our resource-constrained setting.

Conclusion

Our study shows that parathyroidectomy for PHPT is performed safely and effectively at TBH, and the cure and complication rates are comparable to those published in international studies. It highlights the high incidence of advanced disease in our patient population, who present with multiple indications for surgery and are at high risk of developing postoperative HBS. Early disease is often missed due to patients not experiencing any symptoms. When asymptomatic PHPT is detected, early surgical intervention should be considered to avoid

deterioration and long-term complications. Preoperative localisation of the pathological parathyroid gland remains challenging. Implementing 4D CT as a first-line imaging modality instead of only when other methods have failed might improve the detection rate. F-18 Fluorocholine PET/CT, while a promising option, is currently not available in SA and might be cost-prohibitive in our resource-limited setting. Lastly, this study highlights the importance of diligent documentation of patient data, not only for clinical and medicolegal purposes but also for research and quality control.

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ORCID

R Pargner http://orcid.org/0009-0002-3496-7562

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