Wits Journal of Clinical Medicine, 2021, 3(2) 93–100 http://dx.doi.org/10.18772/26180197.2021.v3n2a1

Research Article

A Retrospective Audit of Single Versus Multigland Disease in Primary Hyperparathyroidism at a Single Centre in South Africa

Nicola Amy MacRobert, Deirdré Kruger and Markus Schamm

Department of Surgery, School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

**Correspondence to: Deirdré Kruger Department of Surgery, School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand, 7 York Road, Parktown, 2193 Johannesburg, South Africa. deirdre.kruger@wits.ac.za*
Telephone number : +27-11-717-2376. Fax number: +27-11-484-2717.
Co-authors: Nicola Amy MacRobert, macrobertnicola@gmail.com; Markus Schamm, drschamm@gmail.com

ABSTRACT

Background: Primary hyperparathyroidism (PHPT) is caused by excessive parathyroid hormone production by autonomously functioning parathyroid gland(s), most commonly by adenomatous change in a single gland (SG). This pathological SG may be removed in a minimally invasive surgical approach rather than a traditional bilateral neck exploration. However, this requires the SG to be localized preoperatively using imaging.

Objectives: To determine the prevalence of SG and multigland (MG) disease, techniques used to localize disease preoperatively and outcome based on surgical approach, in patients with PHPT undergoing first parathyroidectomy at the Wits Donald Gordon Medical Centre, Johannesburg, South Africa.

Methods: A retrospective review of all eligible patients (from October 2008 to January 2018) with biochemically confirmed PHPT undergoing parathyroidectomy was conducted.

Results: Records of 252 patients with PHPT were reviewed. SG disease was the cause of PHPT in 83.3% of patients, whereas MG disease, including double adenomas and hyperplastic change, accounted for the remainder. A neck ultrasound scan (USS) was performed in 71.8% of patients with a sensitivity of 77.1% (95% CI, 68.5–84.4%), while 75.4% had a Tc-99 Sestamibi Single -Photon Emission Computed Tomography (SPECT) scan with a comparable sensitivity of 72.9% (63.9–80.7%) in localizing SG disease. Combined USS and SPECT scan had sensitivity in SG disease of 79.7% (71.3–86.5%). Only 44.8% of patients underwent a minimally invasive parathyroidectomy.

Conclusion: A bilateral neck exploration has been the gold standard surgical approach in PHPT management. However, given the predominance of SG disease, with a careful interpretation of reliable preoperative localization imaging studies, a minimally invasive parathyroidectomy should be considered.

Keywords: Hyperparathyroidism, Surgical approach, Single gland, Preoperative imaging

INTRODUCTION

Primary hyperparathyroidism (PHPT) is an endocrine disorder arising from dysregulated parathyroid hormone (PTH) production. Symptoms are caused by the resultant hypercalcaemia. Typically, PHPT affects middle-aged, post-menopausal females.(1) PHPT is diagnosed biochemically by hypercalcaemia in the setting of an inappropriately elevated PTH level. Autonomous PTH production arises from a single parathyroid gland, so-called single gland (SG) disease, in approximately 85% of patients with PHPT.(2) Adenomatous change is usually the underlying pathological change seen in SG disease. Hyperplasia, however, is mainly responsible for MG disease, which occurs in approximately 15% of PHPT patients. Hyperplastic glands are smaller and less impressive than glands enlarged by adenomatous change. Multiple adenomas may also be found in MG disease. Carcinoma is rarely implicated in PHPT (<1%).(2)

PHPT can be cured and is primarily managed by an expedient surgical removal of the pathological gland(s).(3) Traditionally, the surgeon's gold standard involves a bilateral neck exploration in which all four parathyroid glands are explored and any abnormally enlarged gland resected. This approach has cure rates above 95% and does not fundamentally require preoperative imaging.(4) Postoperative cure is defined as normocalcaemia at 6 months post-surgery. However, given that most patients with PHPT have SG disease this has led to an advocacy for a more focused and minimally invasive approach directed at removing the single pathological gland. Comparable successful cure rates of more than 95% have been reported to those achieved with a bilateral neck exploration.(5) In addition, a minimally invasive approach has a smaller and thus more cosmetically appealing scar, shorter operative time and hospital stay, and reduced postoperative complications, such as hypocalcaemia and recurrent laryngeal nerve damage.(6,7)

To remove an SG in a focused surgical manner, the surgeon has to be able to preoperatively localize it. Imaging modalities are used to localize the gland and not to confirm or exclude the diagnosis of PHPT.(8) Commonly used imaging modalities include a neck ultrasound scan (USS) and a Technetium (Tc)-99 Sestamibi single-photon emission computed tomography (SPECT) scan. A neck USS has the advantage of being widely available, cheap and easy to use. However, the success in localizing the gland is often operator dependent.(9) A 2012 meta-analysis reported a pooled sensitivity of a neck USS to be 76.1% (95% CI 70.4–81.4%) with a pooled positive predictive value in SG detection of 93.2% (95% CI 90.7–95.3%). The pooled sensitivity and positive predictive value of a Tc-99 Sestamibi SPECT scan were reported as 78.9% (95% CI 64–90.6%) and 90.7% (95% CI 83.5–96.0%), respectively, for SG disease.(10) However, the latter modality is not widely available, less cost-effective than USS and requires more skill to interpret.(11) Combining the two imaging modalities has been shown to increase preoperative localization accuracy to a sensitivity between 79 and 95% and thus a combined imaging approach is recommended.(12)

Both neck USS and Tc-99 Sestamibi SPECT scans, unfortunately, perform poorly in detecting MG disease.(13,14) Indeed, negative, equivocal or discordant imaging results should raise the suspicion of MG disease and necessitate a bilateral neck exploration.(15) Missed MG disease is a preventable cause of persistent or recurrent hypercalcaemia and, therefore, of 'surgical failure' postoperatively.(16,17) Such an outcome may lead to ongoing target organ damage from hypercalcaemia, in which case a re-exploration is indicated. Re-exploration is technically more challenging and is associated with increased surgical morbidity.(18)

In addition to imaging, other proposed markers of potential use to differentiate SG and MG diseases preoperatively include the degree of clinical symptomatology and elevation of hypercalcaemia, both of which are of a worse degree in adenomatous rather than hyperplastic disease.(19) However, studies have shown inconsistent results using these variables and the widespread clinical use of such strategies has not gained popularity.(13,20) Vitamin D, commonly deficient in the African populations,(21) is a known contributing factor to severity of disease and accuracy of preoperative localization. Ideally, vitamin D levels should be measured in patients with suspected PHPT.(22)

There are no published studies from developing countries that have assessed the value of imaging and other factors in the localization of disease. We thus reviewed a large cohort of patients with PHPT who underwent parathyroidectomy and aimed to determine the predominance of SG disease and whether SG disease can be predicted preoperatively by means of biochemistry and imaging modalities.

MATERIALS AND METHODS

Patient selection

Data from patients of 18 years and older undergoing parathyroidectomy for PHPT at the WITS Donald Gordon Medical Centre in Gauteng, South Africa by a single surgeon over the study period of October 2008 to April 2017 were collected retrospectively. Patients undergoing reoperation and those undergoing parathyroidectomy for renal-related or multiple endocrine neoplasia parathyroid disease were excluded.

Data acquisition

All data were recorded in a REDCap database. Data were anonymized to ensure patient confidentiality and included basic demographic characteristics and relevant biochemistry results of preoperative corrected serum calcium, PTH and vitamin D levels. Also, postoperative serum corrected calcium results were recorded. Preoperative biochemistry done more than 180 days pre-surgery was excluded. Six-month follow-up blood results outside of 7 months post-surgery were also excluded. Hypercalcaemia was defined as a calcium level above 2.60 mmol/L and normocalcaemia as a calcium level of 2.00–2.60 mmol/L.

Preoperative imaging results from neck USS and Tc-99 Sestamibi SPECT were reviewed. SG or MG disease was determined from the number of glands identified by each of these imaging modalities individually and combined. For the use of both imaging modalities together, patients were classified as having MG disease if one or both imaging modalities identified MG disease; otherwise patients were classified as having SG disease.

Classifications based on imaging modalities were then compared to the 'true' or gold standard classification based on surgical and histological assessment. Therefore, a true positive imaging result of SG disease was based on the surgical and histological assessment showing only an SG as pathologically abnormal. Specifically, histological outcome was defined as follows: if one abnormal gland was identified, regardless of whether this was an adenoma, carcinoma or hyperplasia, this was diagnosed as SG disease. If more than one abnormal gland was identified, a diagnosis of MG disease was made. The study fulfilled all the ethical requirements of the University of the Witwatersrand's Human Research Ethics Committee.

Statistical analysis

Data analysis was carried out using SAS version 9.4 for Windows and STATA version 14.2. Descriptive statistics were conducted, and categorical variables were summarized by frequency and percentage, whilst continuous variables were described according to the median and interquartile range (IQR). The associations between preoperative calcium levels and histological outcome, surgery and histological outcome, and between SG/MG disease and adenoma/hyperplasia were determined by the Mann–Whitney *U* Test and chi-squared or Fisher's exact test, as appropriate. Where both imaging tests were carried out, the degree of agreement between neck USS and Tc-99 Sestamibi SPECT scan in the identification of SG versus MG disease was determined by Cohen's kappa with a standard error (SE). The sensitivity and specificity of the individual imaging modalities and their combination in predicting SG and MG diseases are reported. A *P* value of 0.05 was used for statistical significance for all tests.

RESULTS

Patient characteristics and preoperative biochemistry

A total of 252 patients underwent parathyroidectomy during the study period and were included in the study. Table 1 shows the demographic characteristics, preoperative biochemistry and histopathology findings in SG versus MG disease. The median age (IQR) of the study patients at surgery was 60.0 (51.0–70.0) years and this did not differ between SG and MG diseases. The majority of study patients were female (n = 195, 77.4%), regardless of whether SG or MG disease was diagnosed. Histologically proven SG disease was found in 83.3% of patients and adenoma was the causative pathology in 91.0% of these patients. Histologically proven MG disease was found in 13.1% of patients and hyperplasia was the causative pathology in 87.9% of these patients. Nine patients had no glands identified on histology, i.e. tissue mistaken for parathyroid tissue was removed at the time of surgery.

One or more blood results were recorded for 212 patients (15.9% missing data). The median (IQR) preoperative calcium level in the study patients was 2.68 (2.57–2.80) mmol/L and 68.6% (n = 142) had hypercalcaemia (Table 1). The median calcium level was significantly higher in SG versus MG patients (P = 0.03). PTH levels showed a median (IQR) level of 118.6 (88–175) pg/mL, with 93% of patients having PTH levels above the normal range of 15.0–68.3 pg/mL, and none below the normal range. Also, PTH levels were significantly higher in MG versus SG disease patients (P = 0.007). Vitamin D levels were only available in 51% of study patients (n = 128) and did not show any significant differences between SG and MG diseases.

Table 1: Patient demographics, preoperative clinical characteristics and histopathology in Single gland (SG) versus Multigland (MG) disease

Parameters	Total	SG	MG	*P* value*
Study patients, *n* (%)	**252 (100%)**	**210 (83.3%)**	**33 (13.1%)**	
Glands identified	**243 (96.4%)**			
Age, years	60.0 (51.0–70.0)	60.0 (51.0–70.0)	59.0 (48.0–67.0)	0.41
Female, *n* (%)	195 (77.4%)	165 (78.6%)	24 (72.7%)	0.50
Calcium, mmol/L	2.68 (2.57–2.80)	2.70 (2.58–2.83)	2.64 (2.49–2.71)	**0.03**
Calcium level categories (n=207)				
Normocalcaemia, *n* (%)	65 (31.4%)	50 (29.6%)	11 (37.9%)	0.39
Hypercalcaemia, *n* (%)	142 (68.6%)	119 (70.4%)	18 (62.1%)	
PTH, pg/mL	118.6 (88.0–175.0)	116.1 (87.1–166.8)	142.0 (108.0–1102)	**0.007**
Vitamin D, ng/mL	22.1 (16.8–28.5)	21.9 (16.5–28.5)	23.6 (19.8–28.5)	0.56
***Histopathology, n* (%)**				
Adenoma	199 (79.0%)	191 (91.0%)	8 (24.2%)	**<0.0001**
Hyperplasia	42 (16.7%)	17 (8.1%)	29 (87.9%)	**<0.0001**
Carcinoma	2 (0.8%)	2 (0.9%)	0	–
No glands	*9 (3.6%)*			

*Mann–Whitney test statistic for continuous variables; chi^2/Fisher's exact test statistic for categorical variables. Continuous variables are presented as median (interquartile range [IQR]), unless specified otherwise. Categorical variables are expressed as absolute and relative frequencies. PTH, parathyroid hormone. Bold *P* values denote statistical significance at the P < 0.05 level.

Localization of disease with preoperative imaging

Of the 252 patients, 94% (*n* = 237) had at least one type of preoperative imaging performed. A neck USS (Table 2) was performed in 71.8% (*n* = 181) patients. Of these patients, 76.8% were found to have SG disease, 7.2% MG disease and 16.0% had no glands identified. A Tc-99 Sestamibi SPECT scan was performed on 75.4% (*n* = 190) patients, identifying SG and MG diseases in 76.8% and 5.3%, respectively. No glands were identified in 17.9% of patients. Combined imaging was done in 53.2% (*n* = 134) patients. The following results were obtained: 80.6% SG, 12.7% MG and no glands in 6.7% of patients.

To determine the degree of agreement between the neck USS and the Tc-99 Sestamibi SPECT scan in identifying SG and MG diseases, Cohen's kappa (SE) was calculated to be 0.139 (0.07), suggesting poor agreement. For those 134 patients who had both the neck USS and the Tc-99 Sestamibi SPECT scan, the sensitivity and specificity of each imaging modality and their combination in successfully identifying SG or MG disease is shown in Table 3. Preoperative imaging was reasonably sensitive in detecting SG disease but not for the detection of MG disease, albeit reliably specific in the latter.

Surgical approach

The 252 patients had a total of 266 surgeries: 1 patient had 3 surgeries and 12 patients had 2 surgeries each. There were no deaths. For this study, only the first surgery was considered, as these relate directly to the preoperative imaging data. Minimally invasive or unilateral surgery was performed in only 44.8% (*n* = 113) of patients, while the rest had bilateral neck explorations. SG disease as determined by histological outcome was found in 74.1% (*n* = 103) of patients who underwent bilateral four gland exploration.

Postoperative calcium levels

As 6-monthly postoperative serum calcium levels were only available in 21 patients (91.7% missing data), the incidence

Table 2: SG and MG diseases according to imaging modalities

Variable	Total	Histology outcome		
	(*n* = 252)	SG (*n* = 210)	MG (*n* = 33)	No glands(*n* = 9)
Neck USS done, *n* (%)	**181 (71.8%)**	**155 (73.8%)**	**20 (60.6%)**	**6 (66.7%)**
No glands	29 (16.0%)	26 (16.8%)	2 (10%)	**1 (11.1%)**
SG disease	139 (76.8%)	**120 (77.4%)**	14 (42.4%)	5 (55.6%)
MG disease	13 (7.2%)	9 (5.8%)	**4 (12.1%)**	0 (0%)
Tc-99 Sestamibi SPECT done, *n* (%)	**190 (75.4%)**	**167 (79.5%)**	**16 (48.5%)**	**7 (77.8%)**
No glands	34 (17.9%)	29 (17.4%)	4 (25.0%)	**1 (11.1%)**
SG disease	146 (76.8%)	**129 (77.2%)**	11 (68.8%)	6 (66.7%)
MG disease	10 (5.3%)	9 (5.4%)	**1 (6.3%)**	0 (0%)
Both USS and Tc-99 Sestamibi SPECT, *n* (%)	**134 (53.2%)**	**118 (56.2%)**	**12 (36.4%)**	**4 (44.4%)**
No glands	9 (6.7%)	9 (7.6%)	0 (0%)	**0 (0%)**
SG disease	108 (80.6%)	**94 (79.7%)**	10 (83.3%)	4 (100%)
MG disease	17 (12.7%)	15 (12.7%)	**2 (16.7%)**	0 (0%)

MG, multigland; SG, single gland; USS, ultrasound. Bold boxed values denote the % agreement between pre-operative imaging and histology outcome.

Table 3: Sensitivity and specificity of individual and combined imaging modalities

Imaging modality	To identify SG		To identify MG	
(*n* = 134)	Sensitivity % (95% CI)	Specificity % (95% CI)	Sensitivity % (95% CI)	Specificity % (95% CI)
Neck USS	77.1 (68.5–84.4)	31.3 (11.0–58.7)	16.7 (2.1–48.4)	95.1 (89.6–98.2)
Tc-99 Sest. SPECT	72.9 (63.9–80.7)	31.3 (11.0–58.7)	0.0 (0.0–26.5)	92.6 (86.5–96.6)
Both modalities	79.7 (71.3–86.5)	12.5 (1.6–38.4)	16.7 (2.1–48.4)	87.7 (80.5–93.0)

Sest., Sestamibi; USS, ultrasound.

of postoperative normocalcaemia and, therefore, surgical cure rates at 6 months could not be determined retrospectively. Nevertheless, the serum calcium levels immediately postoperatively were available in 157 patients with SG disease (74.8%) and in 27 patients with MG disease (81.8%). In these 157 patients, preoperative hypercalcaemia was present in 109 patients with SG disease (69.4%) and was significantly reduced to only 15 patients (9.6%) postoperatively (P = 0.02), as shown in Figure 1. In the 27 patients with MG disease and postoperative calcium levels available, hypercalcaemia was present in 16 patients (59.3%) preoperatively and only 1 patient (3.7%) remained hypercalcaemic postoperatively, although this reduction was not statistically significant (P = 0.60).

Postoperative PTH levels

In patients with SG disease who had both pre- and immediate postoperative PTH levels measured (n = 155), there was a marked decrease in median PTH level postoperatively. Where 92.2% of SG patients had preoperative PTH levels above the normal range of 68.3 pg/mL compared to only 10.3% postoperatively, this did not reach statistical significance (P = 0.16; Figure 2). The latter may be explained by

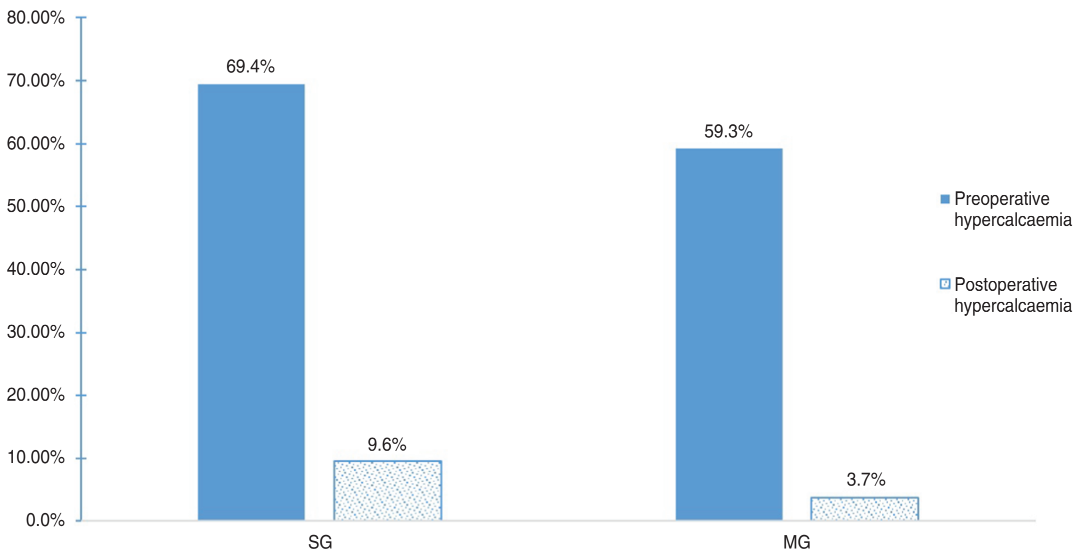


Fig 1: Reduction in hypercalcaemia postoperatively. MG, multigland; SG, single gland

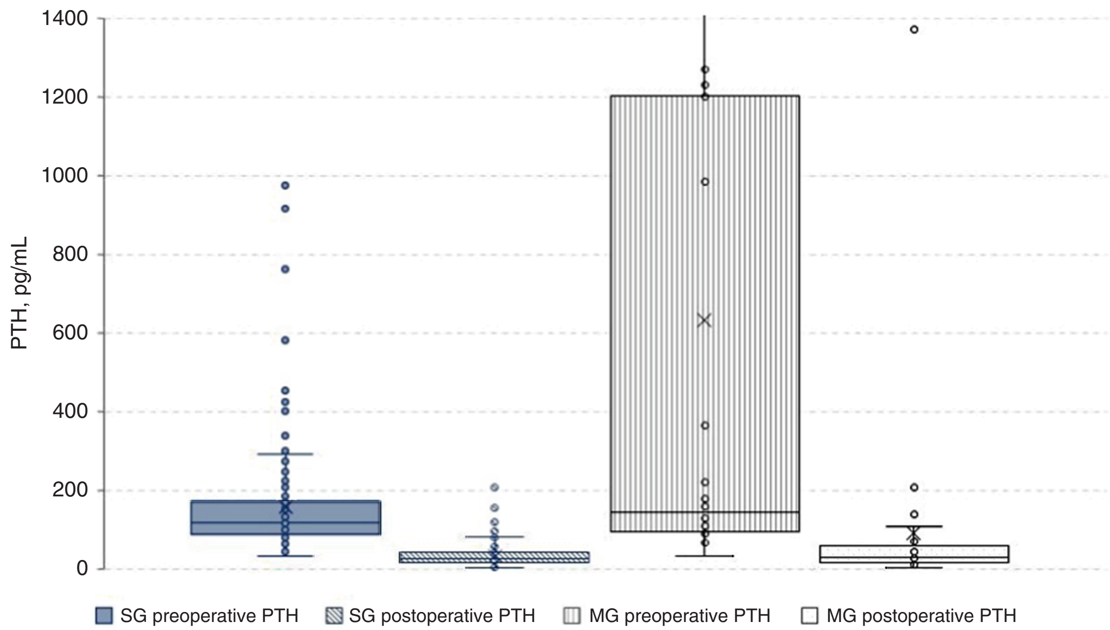


Fig 2: Reduction in PTH levels postoperatively. MG, multigland; PTH, parathyroid hormone; SG, single gland

the eight patients who actually had an increase in postoperative PTH levels; of these eight patients, one also became hypercalcaemic postoperatively. In MG patients with both pre- and postoperative PTH levels available (n = 27), there was a statistically significant decrease in median PTH level postoperatively (P < 0.001; Figure 2).

DISCUSSION

Patients undergoing parathyroidectomy in this cohort from a private academic hospital in Johannesburg, South Africa, had a similar demographic profile to what has been described in the existing literature in that PHPT is mainly a disease of postmenopausal females. Likewise, SG disease was the predominant (83.3%) cause of PHPT and characteristically secondary to adenomatous change.

Preoperative serum corrected calcium and PTH levels are routinely measured in the diagnostic evaluation of a patient with PHPT. Hypercalcaemia was present in 68.6% of the study group while the normocalcaemic phenotype of PHPT was observed in as many as 31.4%. The higher prevalence of the normocalcaemic phenotype of PHPT compared to previously studied, mainly Western population groups,(23) is of interest and may be explained by a possible underlying vitamin D deficiency.(24) Most of the observed vitamin D levels in the study group were in the low normal range.

Although the degree of hypercalcaemia was significantly higher in patients with SG disease compared to MG PHPT, the clinical relevance may not be important as there was a close numerical similarity between the median calcium levels in SG 2.70 mmol/L and MG disease 2.64 mmol/L. Interestingly, MG disease was associated with significantly higher PTH levels, unlike the existing literature where the opposite has been demonstrated.(19) Given this conflicting finding, we caution the application of preoperative biochemistry to clinical practice in predicting SG versus MG disease.

A minimally invasive parathyroidectomy relies upon the accurate preoperative localization of SG disease by using imaging. At least one modality of imaging was performed preoperatively in the majority of patients, a neck USS in 71.8% and a Tc-99 Sestamibi SPECT in 75.4% of the group. Just over half (53.2%) had both forms of imaging done. The study showed a comparable sensitivity, 77.4% for neck USS and 77.2% for Tc-99 Sestamibi SPECT, for the detection of SG disease to what has been reported in the past. Combined imaging resulted in a marginally higher sensitivity (79.7%) for SG disease. However, the agreement between the two imaging modalities was poor and therefore, imaging results, should always be interpreted with caution. Therefore, imaging results must be reviewed by the operating surgeon and the concordance between different modalities established. The sensitivity of detecting MG disease was dismally poor for both neck USS and Tc-99 Sestamibi SPECT. Any discordance or equivocal imaging results should favour a bilateral neck exploration.

Despite the predominance of SG disease and acceptable preoperative localization technique accuracy, only 44.8% (n = 113) of the cohort had a minimally invasive parathyroidectomy. Of those patients who had a bilateral neck exploration, the majority, 74.1% (n = 103), had SG disease on final histopathological review. On temporal analysis of the data, there appeared to be a greater reliance on minimally invasive surgery for SG disease over later years, suggesting that increasing surgical experience may have been a factor. However, a recent retrospective study in the Collaborative Endocrine Surgery Quality Improvement Program, which included more than 5500 patients undergoing a first parathyroidectomy, demonstrated that despite excellent preoperative localization to SG disease, up to 40% of the patients still underwent a four gland exploration, a decision largely at the discretion of the surgeon.(25)

Surgical cure at 6 months between the two operative approaches could not be determined given the large number of missing 6-month postoperative calcium levels. Nevertheless, the analysis of serum calcium levels immediately postoperative showed a clear reduction in the number of patients who remained hypercalcaemic. Likewise, PTH levels dropped dramatically postoperatively. This demonstrates the effectiveness of parathyroidectomy in reversing the biochemical changes in patients with PHPT.

This study does, however, have limitations. First, this is a retrospective study and therefore not all data points were available for each study patient. Second, this study could not investigate whether any association exists between symptomatology and SG or MG disease as this information was not available retrospectively. Finally, this is a single-centre study, and all patients were operated on by a single surgeon and thus the surgical approach possibly reflects a single-operator bias.

CONCLUSION

The biochemical changes characteristic of PHPT, namely hypercalcaemia and hyperparathyroidism, are rapidly reversed with parathyroidectomy. Currently a bilateral neck exploration remains the gold standard surgical approach. However, given the predominance of SG disease in patients with PHPT, a minimally invasive parathyroidectomy based on the accurate interpretation of reliable preoperative localization studies is equally advocated.

Authors' contributions: Nicola MacRobert contributed to study design, collected and interpreted data, drafted the manuscript and approved the final version. Deirdré Kruger contributed to the study design, analysed and interpreted data, critically revised the manuscript and approved the final version. Markus Schamm conceived and designed the study, revised the manuscript and approved the final version.

ACKNOWLEDGEMENTS

The authors express their sincere thanks to the following colleagues from the Wits Donald Gordon Medical Centre for their contributions to this project: Dr Alan Cairns, Professor Simon Naylor and Dr Steve Brachmeyer.

REFERENCES

1. Silva BC, Cusano NE, Bilezikian JP. Primary hyperparathyroidism. Best Pract Res Clin Endocrinol Metab. 2018; 32(5):593–607.
2. Ruda JM, Hollenbeak CS, Stack Jr. BC. A systematic review of the diagnosis and treatment of primary hyperparathyroidism from 1995 to 2003. Otolaryngol Head Neck Surg. 2005; 132(3):359–372.
3. Wilhelm SM, et al. The American Association of Endocrine Surgeons Guidelines for definitive management of primary hyperparathyroidism. JAMA Surg. 2016; 151(10):959–968.
4. Ishii H, et al. Systematic review of cure and recurrence rates following minimally invasive parathyroidectomy. BJS Open. 2018; 2(6):364–370.
5. Udelsman R. Six hundred fifty-six consecutive explorations for primary hyperparathyroidism. Ann Surg. 2002; 235(5):665–70; discussion 670-2.
6. Udelsman R, Lin Z, Donovan P. The superiority of minimally invasive parathyroidectomy based on 1650 consecutive patients with primary hyperparathyroidism. Ann Surg. 2011; 253(3):585–591.
7. Jinih M, et al. Focused versus bilateral parathyroid exploration for primary hyperparathyroidism: a systematic review and meta-analysis. Ann Surg Oncol. 2017; 24(7):1924–1934.
8. Machado NN, Wilhelm SM. Diagnosis and evaluation of primary hyperparathyroidism. Surg Clin North Am. 2019; 99(4):649–666.
9. Patel CN, et al. Clinical utility of ultrasound and 99mTc Sestamibi SPECT/CT for preoperative localization of parathyroid adenoma in patients with primary hyperparathyroidism. Clin Radiol. 2010; 65(4):278–287.
10. Cheung K, et al. A meta-analysis of preoperative localization techniques for patients with primary hyperparathyroidism. Ann Surg Oncol. 2012; 19(2):577–583.
11. Wang TS, et al. Would scan, but which scan? A cost-utility analysis to optimize preoperative imaging for primary hyperparathyroidism. Surgery. 2011; 150(6):1286–1294.
12. Tawfik AI, et al. Added value of ultrasonography and Tc-99m MIBI SPECT/CT combined protocol in preoperative evaluation of parathyroid adenoma. Eur J Radiol Open. 2019; 6:336–342.
13. McHenry CR, Shi HH. Can parathyroid hyperplasia be predicted preoperatively?. Am J Surg. 2018; 215(3):389–392.
14. Xue J, et al. Comparison between technetium-99m methoxyisobutylisonitrile scintigraphy and ultrasound in the diagnosis of parathyroid adenoma and parathyroid hyperplasia. Nucl Med Commun. 2018; 39(12):1129–1137.
15. Treglia G, et al. Imaging in primary hyperparathyroidism: focus on the evidence-based diagnostic performance of different methods. Minerva Endocrinol. 2018; 43(2):133–143.
16. Alhefdhi A, et al. Recurrent and persistence primary hyperparathyroidism occurs more frequently in patients with double adenomas. J Surg Res. 2014; 190(1):198–202.
17. Patel SG, et al. Multimodal preoperative localization improves outcomes in reoperative parathyroidectomy: a 25-year surgical experience. Am Surg. 2019; 85(9):939–943.
18. Weber CJ, Sewell CW, McGarity WC. Persistent and recurrent sporadic primary hyperparathyroidism: histopathology, complications, and results of reoperation. Surgery. 1994; 116(6):991–998.
19. Kebebew E, et al. Predictors of single-gland vs multigland parathyroid disease in primary hyperparathyroidism: a simple and accurate scoring model. Arch Surg. 2006; 141(8): 777–782; discussion 782.
20. Lim JY, et al. Differences in single gland and multigland disease are seen in low biochemical profile primary hyperparathyroidism. Surgery. 2017; 161(1):70–77.
21. Mogire RM, et al. Prevalence of vitamin D deficiency in Africa: a systematic review and meta-analysis. Lancet Glob Health. 2020; 8(1):e134–e142.
22. Tay YD, et al. Pre-operative localization of abnormal parathyroid tissue by (99m)Tc-Sestamibi in primary hyperparathyroidism using four-quadrant site analysis: an evaluation of the predictive value of vitamin D deficiency. Endocrine. 2018; 60(1):36–45.
23. Gomez-Ramirez J, Mihai R. Normocalcaemic primary hyperparathyroidism: a diagnostic and therapeutic algorithm. Langenbecks Arch Surg. 2017; 402(7):1103–1108.
24. Babwah F, Buch HN. Normocalcaemic primary hyperparathyroidism: a pragmatic approach. J Clin Pathol. 2018; 71(4):291–297.
25. Kiernan CM, et al. Bilateral neck exploration for sporadic primary hyperparathyroidism: use patterns in 5,597 patients undergoing parathyroidectomy in the collaborative endocrine surgery quality improvement program. J Am Coll Surg. 2019; 228(4):652–659.

ONYX ONE
THE ONLY ONE

Resolute Onyx™ DES was shown to be safe and effective in highly complex high bleeding risk (HBR) patients with 1-month DAPT.[1]

Resolute Onyx™ DES

Resolute Onyx DES
Non-inferior to
BioFreedom™* DCS†

Superior Acute Performance with
Resolute Onyx DES**

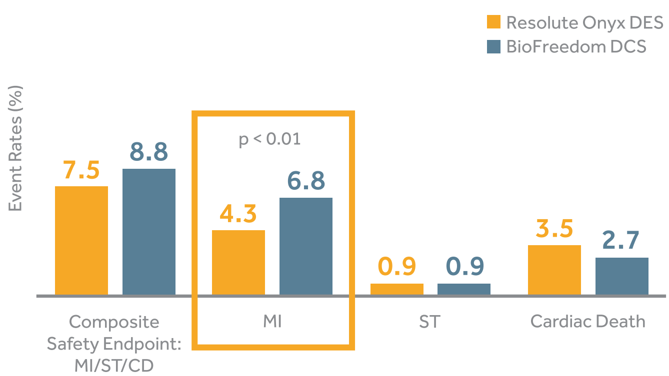
HIGHLY COMPLEX PATIENT POPULATION

53%	80%	33%
ACS	B2/C LESIONS	AF

Low event rates for Resolute Onyx DES

in a highly complex patient population, including significantly lower MI vs. BioFreedom DCS.††

LANDMARK ANALYSIS AFTER DAPT DISCONTINUATION***



*Third-party brands are trademarks of their respective owners.
†At one year.
**Acute performance parameters were not powered or adjusted for multiplicity.
††Post-hoc analyses were not powered.
***From 1 month to 1 year.
[1] Windecker, et al. Data presented at TCT 2019; San Francisco, CA.

medtronic.com

Medtronic