Ultrasonography alone can reliably locate parathyroid tumours and facilitates minimally invasive parathyroidectomy

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ABSTRACT

INTRODUCTION Minimally invasive parathyroidectomy (MIP) is performed via a short incision (≤ 3 cm). Previous studies have employed multiple imaging modalities including ultrasonography, sestamibi imaging and/or intraoperative parathyroid hormone assay. We present our eight-year experience of MIP using ultrasonography alone.

METHODS One hundred parathyroidectomies performed by a single surgeon between April 2004 and December 2012 were identified in a prospectively maintained database. All patients underwent ultrasonography including preoperative marking of the lesion by a single radiologist. No other localising diagnostic tests were performed.

RESULTS Of the 100 patients (69% female) who underwent parathyroidectomy, 93 had MIP. The median age of all cases was 58 years (range: 19–90 years). All patients exhibited an elevated parathyroid hormone level (median: 19pmol) in the presence of hypercalcaemia (median: 2.86mmol/l, range: 2.54–3.94mmol/l). Conventional surgery was indicated in seven patients owing to the need for concurrent thyroidectomy. The median operative time was 30 minutes (range: 10–130 minutes). Ultrasonography localised parathyroid tumour position correctly in 98% of patients who underwent MIP, and in 97% across both MIP and non-MIP groups. Postoperative complications requiring treatment included pancreatitis and symptomatic hypocalcaemia. Follow-up review at 6–8 weeks demonstrated that 86% of open cases (6/7) and 94% of MIP cases (87/93) were rendered normocalcaemic.

CONCLUSIONS Our study is the first to demonstrate that the sole use of ultrasonography including preoperative marking can localise parathyroid tumours correctly in 98% of cases suitable for MIP.

KEYWORDS

Minimally invasive – Parathyroidectomy – Ultrasonography – Parathyroid glands – Surgical procedures

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Symptomatic hypercalcaemia most often results from primary hyperparathyroidism owing to aberrant parathyroid hormone secretion and occurs in approximately 1% of the population. Incidence is age dependent, varying from 10 per 100,000 individuals under 40 years old and increasing to 40 per 100,000 in those over 60 years old.¹ Curative treatment traditionally involved parathyroidectomy by collar incision as pioneered by Felix Mandl in 1925, allowing four-gland exploration with a high success rate and a hospital stay of 2–3 days.² However, close to 90% of cases of primary hyperparathyroidism are attributable to an isolated parathyroid adenoma.¹ It is for this reason that targeted single gland excision by minimally invasive parathyroidectomy (MIP) has gained popularity since the 1990s. The benefits conferred by such a technique are a smaller incision, and reduced tissue dissection and operative time. Consequent improvements in cosmesis, postoperative pain and reduced hospital stay have also been reported.³

Although MIP is most commonly performed by focused lateral mini-incision, other MIP techniques comprising endoscopic and radioguided approaches have been used.^{4–7} Regardless of the operative approach, MIP requires optimal parathyroid adenoma localisation studies to be efficacious.

Previous centres have employed the combination of multiple imaging modalities including ultrasonography, sestamibi imaging and computed tomography (CT). A meta-analysis from 2012 including 43 studies suggested that the positive predictive value of ultrasonography (93.2%) is comparable with both sestamibi single photon emission computed tomography (90.7%) and four-dimensional CT (93.5%).⁸ Nevertheless, the sensitivity of ultrasonography and sestamibi investigations in multiglandular disease or hyperplasia has been as low as 60%, particularly when ultrasonography is compromised by thyroid multinodular disease, challenging adenoma detection.^{9,10} Biochemical and histological adjuncts to radiological imaging have also

been employed including intraoperative parathyroid hormone assay, methylene blue uptake and frozen section.¹¹ In view of the ongoing debate regarding the optimal imaging strategy, we present our eight-year retrospective experience of MIP using ultrasonography alone.

Methods

One hundred parathyroidectomies performed by a single surgeon between April 2004 and December 2012 were identified in a prospectively maintained database. All patients underwent outpatient ultrasonography by a single radiologist. This was followed by preoperative ultrasonography guided marking of the lesion on the operative day by the same radiologist. No other localising diagnostic tests or intraoperative adjuncts such as parathyroid assay were employed. Unlike other studies, intraoperative imaging via ultrasonography or gamma probe were not implemented concurrently. Patients were followed up in the outpatient clinic at 6–8 weeks, at which time postoperative serum calcium levels with or without parathyroid hormone levels were measured. Biochemical cure was defined as a calcium level of 2.1–2.6mmol/l as per the normal reference range of our biochemistry department.

Ultrasonography

A single consultant radiologist (AB) performed all parathyroid marking imaging. Ultrasonography was performed in the supine position with neck extension. A linear transducer probe (15MHz; GE Healthcare, Chalfont St Giles, UK) was placed transversely and longitudinally to locate the enlarged parathyroid gland (Fig 1). Parathyroid glands were identified relative to the thyroid anatomy. Surface marking of the adenoma in relation to the thyroid lobe was performed. Deep adenomas were marked 'deep' to guide surgical exploration.

Operative technique

All MIP cases were performed under general anaesthesia in the supine position with neck extension. An ipsilateral vertical mini-incision of ≤ 3 cm was performed in all cases as guided by ultrasonography marking. Dissection through skin, subcutaneous tissue and platysma with lateral retraction of the sternocleidomastoid was performed to expose the thyroid gland. Medial retraction of the thyroid was followed by identification of the relevant parathyroid gland. The recurrent laryngeal nerve was identified and protected, and excision of the parathyroid gland without capsular breach ensued. Following excision, specimens were sent for conventional histopathology without frozen section. In the event of discovering a normal gland, ipsilateral exploration was performed through the same incision without extension.

Results

A total of 100 patients (69% female) underwent parathyroidectomy and 95 of these were suitable for MIP (Fig 2). The median age of all patients was 58 years (range: 19–90

Figure 1 Transverse (A) and longitudinal (B) views on ultrasonography of a 43-year-old woman with left-sided parathyroid adenoma (arrow) and thyroid gland (star)

years). All patients exhibited elevated parathyroid hormone levels in the presence of hypercalcaemia (median: 2.86mmol/l, range: 2.54–3.94mmol/l). Conventional open surgery was indicated in seven patients owing to the presence of bilateral lesions ($n=3$), requirement for a concurrent thyroidectomy ($n=2$), a mediastinal lesion ($n=1$) or re-exploration ($n=1$). A vertical cervical incision of ≤ 3 cm was performed in all MIP cases and the median operative time was 30 minutes.

The localisation accuracy of ultrasonography across both MIP and non-MIP groups was 97%. Ultrasonography localised the parathyroid tumour position correctly in 98% of patients who underwent MIP (91/93). In the two other cases, adenomas were not found in the marked laterality at operation, leading to closure without any gland excision. Postoperative sestamibi imaging showed one adenoma to be on the contralateral side and one to be a complex adenoma with retrosternal extension. In both these cases, adenomas were identified and excised at reoperation (one requiring a formal manubriectomy), resulting in a biochemical cure.

The histological breakdown of the excised lesions is shown in Table 1. All three atypical adenomas and two of the three carcinomas were followed up with six-monthly calcium and parathyroid hormone monitoring. The remaining individual with a carcinoma was readmitted for an ipsilateral thyroid lobectomy because of focal involvement of the previously excised parathyroid carcinoma. All carcinomas were discovered at operation and not suspected preoperatively. Apart from the two cases where initial surgery could not identify an adenoma, only four cases also exhibited persistent hypercalcaemia postoperatively (histology: 1 adenoma, 1 atypical adenoma, 1 normal parathyroid tissue, 1 hyperplastic adenoma). It is assumed that failure of biochemical correction in these cases was due to multiglandular hyperplasia and all individuals, having been better symptomatically, chose to be monitored instead of pursuing further surgery. Overall, the biochemical cure

rate in terms of resolving hypercalcaemia was 94% for the MIP patients (87/93).

Complications and follow-up review

Postoperative minor complications included episodes of hoarse voice ($n=2$) and paraesthesia ($n=11$) in the presence normocalcaemia, which all resolved. Major inpatient complications requiring treatment included one case of acute coronary syndrome, and two cases of symptomatic hypocalcaemia requiring correction with intravenous fluids and calcium gluconate respectively. One case of pancreatitis, a

Table 1 Histological results of the 100 parathyroidectomies

Histology of excised gland	Minimally invasive ($n=93$)	Open ($n=7$)	Total
Typical adenoma	83	4	87
Hyperplastic adenoma	1	3	4*
Atypical adenoma	3	0	3
Carcinoma	3	0	3
Lymph node	1	0	1
Normal parathyroid tissue	2	0	2

*multiple endocrine neoplasia type 1 ($n=3$)

recognised but rare complication of parathyroidectomy,¹² was also encountered.

Discussion

Our study is the first to demonstrate the benefits of MIP preceded by the sole use of ultrasonography including preoperative marking of the lesion. Correct localisation of parathyroid tumours occurred in 98% of cases suitable for MIP. This is comparable with other groups where a 95% accuracy has been reported in detecting intraoperative parathyroid adenomas using a low dose, multiple day technetium (^{99m}Tc) sestamibi protocol.^{13,14} In this protocol, double tracer subtraction ^{99m}Tc sestamibi scintigraphy and neck ultrasonography was performed. Within one week of the scintigraphy, patients underwent radioguided MIP by injecting 37MBq of ^{99m}Tc sestamibi ten minutes before surgery.

We recommend the combination of ultrasonography and MIP as an efficacious method for excision of parathyroid tumours. Our approach expedites the preoperative workup by obviating the need for sestamibi imaging as well as the associated risk of ionising radiation and contrast related morbidity. Indeed, sestamibi imaging in itself has been shown to be equivocal or negative in 12–15% of studies.¹⁵

Our combination of preoperative marking facilitating a focused minimal dissection and avoidance of intraoperative parathyroid assay has resulted in a shorter operative time (median: 30 minutes) than similar studies employing the focused lateral approach (42.38 minutes).¹¹ The expedience of this approach is likely to have a cost benefit. Although we have not performed formal cost effectiveness analysis, the gross disparity in pricing between ultrasonography alone and additional cross-sectional imaging, nuclear imaging and/or laboratory testing suggests our protocol may incur significant cost savings by using ultrasonography alone. We believe this despite each patient requiring two ultrasonography scans: one as an outpatient and an additional more expedient inpatient scan performed for marking the lesion preoperatively. This remains the case even in view of the few cases that required repeat postoperative imaging.

Operative workup has been supplemented previously by invasive preoperative fine needle aspiration of suspected adenomas with high specificity and sensitivity. However, it remains debatable whether the added patient distress, clinic and staff time is feasible for marginal improvements in specificity.¹⁶ Recent interest in the merits of surgeon performed parathyroid ultrasonography has been evident.¹⁷ It has been described in various studies as an appropriate method of parathyroid location and its accuracy has been compared with sestamibi imaging.^{18–20} Apart from the low cost and non-invasiveness, it has been shown to provide accurate anatomic delineation of the adenomas relative to the thyroid gland, carotid artery and the clavicles, thereby facilitating a limited dissection.²¹ Although the reported sensitivity and overall accuracy of identifying abnormal glands reported by Deutmeyer *et al* as 87% and 88% are encouraging for surgeon performed parathyroid ultrasonography,²¹ these remain less accurate than our results.

Advances in ultrasonography technology and increasing availability through inexpensive portable setups are encouraging use beyond the radiology department among the surgical fraternity. Colour Doppler ultrasonography (CDUS), for instance, has been described as increasing the sensitivity and specificity (97% and 100% respectively) in demonstrating a parathyroid adenoma in patients with primary hyperparathyroidism compared with ultrasonography alone.²² Blood is supplied to the parathyroid gland via the inferior thyroid artery and it can be traced through CDUS. A parathyroid adenoma is typically hypervascular in comparison with its adjacent structure and appears as a 'spot of fire'. In our series, CDUS was not performed on any of the patients as unequivocal diagnosis of parathyroid adenoma was made on ultrasonography alone. Nevertheless, in equivocal cases, CDUS may be a useful adjunct to aid diagnosis.

Study limitations

Our retrospective study is limited by the number of cases and the absence of randomised control subjects. In addition, this single centre experience reflects the practice of two highly experienced consultants (surgeon and radiologist) and study findings may therefore not reflect variable diagnostic accuracy in other centres. It is arguable that intraoperative parathyroid hormone assay may be beneficial in recurrent exploration or pre-emptive to conversion cases. However, in our case series, this would have seemingly only benefited three patients, where non-adenomatous tissue was excised (Table 1).

Conclusions

Our study suggests MIP in combination with lone ultrasonography is a safe strategy for diagnosis and treatment of primary hyperparathyroidism in the context of solitary adenoma. This approach is becoming increasingly available to the non-radiologist and may incur further cost savings with dissemination of ultrasonography technique. Prospective analysis is encouraged in the form of randomised controlled studies and formal cost effectiveness analysis.

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