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Efficacy of surgeon-performed, intra-operative ultrasound scan for localisation of parathyroid adenomas in patients with primary hyperparathyroidism

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Abstract

Background. In the UK, guidance recommends ultrasound scanning alone or in combination with sestamibi scintigraphy to guide surgery in patients with primary hyperparathyroidism. If an adenoma is localised on imaging, this can facilitate targeted or minimally invasive surgery. Surgeon-performed ultrasound scan on the operating table benefits from being performed on an anaesthetised patient with optimal positioning. The aim of this study was to investigate the efficacy of intra-operative, blinded, surgeon-performed ultrasound scan in localisation of parathyroid adenomas.

Methods. Prospective data were collected on consecutive patients undergoing surgery for primary hyperparathyroidism at a single tertiary centre from November 2019 to June 2021. Patients underwent blinded, surgeon-performed ultrasound scan under general anaesthesia immediately prior to surgery. Localisation results from pre-operative imaging and surgeon-performed ultrasound scan were then compared with the intra-operative findings.

Results. Forty-nine patients underwent surgery and were found to have single-gland disease. Sestamibi scintigraphy, radiologist-performed ultrasound scan and surgeon-performed ultrasound scan had sensitivities of 59.4, 43.75 and 73.8 per cent, respectively. Surgeon-performed ultrasound scan had a statistically significantly increased sensitivity compared with radiologist-performed ultrasound ($p < 0.05$).

Conclusion. Intra-operative, surgeon-performed ultrasound scan is effective in localising parathyroid adenomas and may be a useful adjunct to facilitate minimally invasive parathyroid surgery.

Introduction

The success of minimally invasive parathyroidectomy is reliant on accurate pre-operative localisation of parathyroid adenomas. It is the treatment of choice in localised, single-gland disease in primary hyperparathyrodisim.[1] A minimally invasive approach has several advantages over bilateral neck exploration, including fewer complications, reduced cost and a shorter in-patient stay.[2]

Imaging modalities for localisation of parathyroid disease include sestamibi scintigraphy, ultrasound scanning, magnetic resonance imaging and four-dimensional computed tomography.[3,4] Current UK guidelines recommend pre-operative ultrasound scanning for all patients with the addition of a second imaging technique, typically a sestamibi scintigraphy scan, if this will aid further surgical management.[1] Specifically, they advise against any further imaging if this initial imaging fails to locate an adenoma or the imaging is discordant.[1]

The sensitivity of radiologist-performed ultrasound in locating abnormal parathyroid glands has been reported as 76.1 per cent with a positive predictive value of 93.2 per cent in a meta-analysis of parathyroid imaging.[5] Radiologist-performed ultrasound is typically performed by a radiologist or ultrasonographer, ideally with an interest in endocrine imaging. This is not always widely available within the UK. Ultrasound is highly user dependent. Varying experience and skill level of radiologist-performed ultrasounds are likely reflected in the broad range of sensitivities reported in the literature.[4,5]

Surgeon-performed ultrasound has been widely adopted in North America and Australasia; they are performed in clinic as part of the pre-operative imaging investigation. Published data from multiple studies show that surgeon-performed ultrasound scan has equivalent, or in some cases superior, sensitivity to radiologist-performed ultrasound.[6–15] Literature from the UK is sparse in comparison, and clinic-based surgeon-performed ultrasound scanning has not been widely adopted. Limited data have reported the benefits of a surgeon-performed ultrasound scan completed immediately prior to surgery in the operating theatre in an anaesthetised patient. There appears to be increased sensitivity of localisation of parathyroid adenomas compared with pre-operative radiologist-performed ultrasound and increased concordance with sestamibi scintigraphy.[16,17]

Main Article

Dr A Habib takes responsibility for the integrity of the content of the paper

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This study aimed to assess the sensitivity of blinded, surgeon-performed ultrasound scan in the operating theatre and compare this with the patient's pre-operative localisation imaging. At our institution, an anaesthetist with a specialist interest in parathyroid disease also performed ultrasound in the operating theatre on the same patients, enabling further comparison with pre-operative radiologist-performed ultrasound. Data were also collated on gland weight, pre-operative calcium levels and final histology.

Materials and methods

This was a prospective observational study over a 2.5-year period from November 2019 to June 2021. All consecutive adult patients who underwent either a minimally invasive parathyroidectomy or a four-gland exploration for primary hyperparathyroidism were included in this study. Surgery was performed by a single experienced parathyroid surgeon (JE). Exclusion criteria included patients with secondary or tertiary hyperparathyroidism and patients undergoing revision surgery. Data regarding surgeon-performed ultrasound scan were recorded at the time of surgery, with pre-operative imaging and histology collated from case notes. Data obtained included patient demographic information, serum parathyroid hormone, serum calcium levels, pre-operative imaging results and local costing for investigations.

A single experienced surgeon performed an ultrasound scan on all patients immediately prior to surgery. The surgeon had attended a head and neck ultrasound course in the UK and had 15 years' overall experience of performing neck ultrasound scans in an out-patient setting. Surgeon-performed ultrasound scan was performed while patients were under general anaesthesia in a supine position with the neck extended using the Sonosite SII UltraSound System (Fujifilm, Amsterdam, The Netherlands; reference: P20883-13). The surgeon was blinded to the results of any pre-operative radiologist-performed ultrasound and sestamibi scintigraphy imaging prior to surgeon-performed ultrasound scan. Separately, ultrasound was also performed by the senior anaesthetist with a specialist interest in parathyroid surgery (CS). These results were recorded separately from surgeon-performed ultrasound scan findings. The anaesthetist was trained in head and neck ultrasonography by the same surgeon who performed the ultrasound scan.

The surgeon subsequently accessed any pre-operative imaging, after recording the results of surgeon-performed ultrasound scan, to facilitate minimally invasive surgery in as many cases as possible. Operative findings were compared with pre-operative imaging and surgeon-performed ultrasound scan to compare sensitivity in localising a parathyroid adenoma.

Results

A total of 49 patients were included in the study. There were 11 males and 38 females. The age range was between 22 and 88 years with a median age of 60 years. Of these, 6 patients underwent a 4-gland exploration, and 43 patients had a minimally invasive surgical approach. All patients had single-gland disease. A total of 37 sestamibi scintigraphy and 22 radiologist-performed ultrasound scans were performed pre-operatively. Of these, 17 patients had double imaging (radiologist-performed ultrasound and sestamibi scintigraphy), and 9 patients had no pre-operative imaging by choice. All 49 patients had surgeon-performed ultrasound scan on the operating table. Nine ectopic glands were identified intra-operatively (five retroesophageal and four paraesophageal). As these would not be expected to be detected on ultrasound, they were not included in the sensitivity analysis of radiologist-performed ultrasound and surgeon-performed ultrasound scans. Patient demographic data and serum calcium levels are summarised in Table 1.

Table 1. Patient demographic data and calcium levels

Parameter	Value
Patients (*n*)	49
Age (mean (range); years)	60 (22–88)
Gender (*n*)	
– Male	11
– Female	38
Serum calcium (*n*)	
– 2.4–2.60 mmol/l	3
– 2.61–2.80 mmol/l	26
– 2.81–3.0 mmol/l	11
– 3.1–3.20 mmol/l	7
– 3.21–3.4 mmol/l	2

Sestamibi scintigraphy correctly identified 22 of 37 adenomas (59.4 per cent), radiologist-performed ultrasound identified 7 of 16 adenomas (43.75 per cent) and surgeon-performed ultrasound scan correctly identified 31 of 42 adenomas (73.8 per cent). A McNemar's test (asymptotic version) was performed and showed a statistically significant difference in sensitivities between surgeon-performed ultrasound scan and radiologist-performed ultrasound ($p < 0.05$). The test did not show a statistically significant difference between surgeon-performed ultrasound scan and sestamibi scintigraphy ($p = 0.16$), although there was a tendency towards improved sensitivity with surgeon-performed ultrasound scan. The sensitivities are shown in Table 2.

Out of the nine ectopic glands, sestamibi scintigraphy correctly identified five adenomas: three were paraesophageal and two were retroesophageal. Sestamibi scintigraphy failed to identify any adenoma in two cases of retroesophageal ectopic adenomas and wrongly identified potential adenomas in two cases.

As would be expected, surgeon-performed ultrasound scan failed to identify any ectopic adenomas in these locations. In 7 of 9 (77.7 per cent) cases of ectopic adenoma, surgeon-performed ultrasound scan correctly had a negative ultrasound finding with no adenoma identified. In two of nine cases, surgeon-performed ultrasound scan incorrectly identified a potential adenoma in an alternative location. Radiologist-performed ultrasound was performed in six of nine cases of ectopic adenoma, and the finding was negative in all cases.

Table 2. Sensitivity of imaging modalities

Imaging modality	Sensitivity (%)
Radiologist-performed ultrasound	43.75
Sestamibi scintigraphy	59.4
Surgeon-performed ultrasound	73.8

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Forty-six patients were confirmed to have an adenoma on histopathological assessment. Two glands were reported as histologically normal although they weighed 530 mg and 440 mg (normal gland weight is 30–50 mg). Unfortunately, one of these patients did not present for any follow up despite numerous attempts to contact them, so we are unable to comment on cure. One histology report showed a parathyroid carcinoma. The cure rate in the sample was 97.8 per cent following surgery. Gland weight was not reported in three cases. There was a mean adenoma weight of 1170 mg and median of 740 mg in 45 patients (range: 26–7200 mg). The location of the glands is summarised in Table 3. No correlation was found between gland weight and detection rate of the adenoma in the sample.

Blinded intra-operative ultrasound was also performed by a senior anaesthetist (CS) with a specialist interest in endocrine surgery. His results showed a sensitivity of 71.4 per cent compared with 73.8 per cent for surgeon-performed ultrasound scan and 43.75 per cent for radiologist-performed ultrasound.

In our trust, the average cost of a neck ultrasound scan incurred by the hospital was £38 per patient with a total cost of £836 for 22 patients. A sestamibi scintigraphy was charged at £1480 per scan with a total of £54 760 for 37 patients. The mean operative time for a minimally invasive approach, including surgeon-performed ultrasound scan in the operating theatre, was 62 minutes, and a 4-gland exploration took 72 minutes.

Discussion

The majority of patients in our series had undergone pre-operative radiologist-performed ultrasound and/or sestamibi scintigraphy as a first-line investigation. The sensitivity of radiologist-performed ultrasound and sestamibi scintigraphy in our series was 43.75 per cent and 59.4 per cent, respectively. These sensitivity figures for radiologist-performed ultrasound and sestamibi scintigraphy are lower than those reported in the meta-analysis by Cheung *et al.* but similar to those reported in a UK-based study.[5,16] This may reflect the lack of dedicated endocrine radiologists.

Surgeon-performed ultrasound scan had a sensitivity of 72.8 per cent compared with 43.75 per cent for radiologist-performed ultrasound. This was statistically significant ($p < 0.05$). The sensitivity of sestamibi scintigraphy localisation in our institution was 59.4 per cent. Surgeon-performed ultrasound scan trended towards improved sensitivity compared with sestamibi scintigraphy, but this did not reach the threshold for statistical significance.

As noted earlier, ultrasound is highly user dependent. The advantages of ultrasound in the operating theatre include an anaesthetised patient and hyperextended position. Surgeon-performed ultrasound scan is performed by a surgeon experienced in parathyroid surgery with a detailed knowledge of the anatomy and likely locations of adenomas.

Table 3. Intra-operative adenoma location

Adenoma location	Patients (*n*)
Right upper neck	7
Right lower neck	13
Left upper neck	5
Left lower neck	15
Ectopic	9

Our results are comparable with previously published sensitivities for surgeon-performed ultrasound scan in the operating theatre as reported by Aspinall *et al.* and Thomas *et al.*[16,17] It is worth noting that our radiologist-performed ultrasound sensitivity of 43.75 per cent is lower than generally reported figures. This may reflect the various clinicians undertaking radiologist-performed ultrasound because they may not be regularly performing endocrine ultrasound at our institution.

Parathyroid adenomas may be found in ectopic locations within the neck. Typical locations include retroesophageal, paraesophageal, intra-thyroid or within the thymus. In our series, nine ectopic adenomas were found in paraesophageal and retroesophageal locations. Because of the location, these would not be expected to be visible on ultrasound but may be identified by sestamibi scintigraphy. Ultrasound has been reported to be able to identify some intra-thyroid ectopic glands, although sestamibi scintigraphy is considered superior for identifying ectopic adenomas overall.[18,19] If performed, a negative ultrasound scan should raise suspicion of an ectopic adenoma.

In our series, the use of surgeon-performed ultrasound scan enabled an additional six patients to undergo minimally invasive parathyroidectomy where pre-operative imaging had failed to localise the adenoma. Surgeon-performed ultrasound scan also allows marking of the location of the adenoma in the surgical position, facilitating a smaller incision and reduced dissection.

Ultrasound is an inexpensive, non-invasive imaging tool that is easily accessible. Although UK surgeons generally have limited training in ultrasonography, it is becoming more common and can be easily obtained. Factors such as obesity, multinodular thyroid goitres, small gland size and ectopic location are all recognised to contribute to reduced identification of adenomas on ultrasound.[20] At our institution, radiologist-performed ultrasound is performed by various clinicians who are not exclusively dedicated to reporting endocrine pathology in the neck. In contrast, the surgeon performing the ultrasound intra-operatively performs a high volume of parathyroid surgical procedures annually.

- The success of minimally invasive parathyroid surgery depends largely on accurate pre-operative localisation of parathyroid adenomas
- UK guidelines recommend pre-operative ultrasound scanning for all patients prior to surgery with further imaging, typically a sestamibi scintigraphy scan, if this will aid surgical management
- Recently, surgeon-performed ultrasound has been widely adopted for pre-operative localisation of parathyroid disease in North America with considerable success
- Data from the UK is sparse as this technique has only been adopted in a few centres
- The current study showed an advantage of surgeon-performed ultrasound in the operating theatre over radiologist-performed ultrasound and a trend towards increased sensitivity over sestamibi scintigraphy
- Surgeon-performed ultrasound may be a useful adjunct to facilitate minimally invasive parathyroid surgery, especially where pre-operative imaging has failed to localise an adenoma

There may be greater benefit to UK practice from surgeon-performed ultrasound scan in the operating theatre than from the more widely reported pre-operative surgeon-performed ultrasound scan. This is particularly so where dedicated endocrine radiologist-performed ultrasound is not available. With regard to training of UK-based otolaryngology registrars in performing a neck ultrasound, attendance at courses dedicated to head and neck ultrasonography and its subsequent use in an out-patient setting would be of great benefit. Besides parathyroid disease, it would aid in the diagnostic investigation of head and neck malignancy as well as salivary gland and thyroid disease.

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This study benefited from being prospective and because of the blinding of the surgeon performing ultrasound scan in the operating theatre. Limitations of this study include data being from a single institution and surgeon-performed ultrasound scan being performed by a single surgeon; therefore, results may not be generalisable. However, the comparable sensitivities also obtained by the senior anaesthetist and other UK studies are encouraging.[16,17]

Appropriately powered, multi-centre studies would be required to determine the widespread applicability and overall additional benefit of surgeon-performed ultrasound scan.

Conclusion

The findings in the study suggest the advantage of surgeon-performed ultrasound scan in the operating theatre over pre-operative radiologist-performed ultrasound and a trend towards increased sensitivity over sestamibi scintigraphy. Surgeon-performed ultrasound scan may be a useful adjunct to facilitate minimally invasive parathyroid surgery, particularly where pre-operative imaging has failed to localise an adenoma or in centres lacking dedicated endocrine radiologist-performed ultrasound.

Competing interests. None declared

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