Audit

Surgical management of primary hyperparathyroidism – results of a national survey

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Background: During the last decade, the surgical management of primary hyperparathyroidism has been limited to those patients with symptoms or complications of the disease and most surgeons have advocated routine bilateral neck exploration. Several recent articles, however, have supported the role of early surgical intervention and minimally invasive surgery for these patients. The aim of this study was to define the current surgical management of primary hyperparathyroidism in the UK and Ireland.

Methods: A postal questionnaire was sent to all consultant members of the British Association of Endocrine Surgeons in November 2000. The surgeons were asked about their current criteria for patient selection, methods of pre-operative localisation, imaging technique before re-exploration, operative technique and follow-up.

Results: Questionnaires were returned from 66 of 92 surgeons (response rate 71.7%) currently performing parathyroid surgery in the UK and Ireland, at an average of 23.1 parathyroidectomies performed per annum (range, 5–120). The majority of patients referred for surgery were either asymptomatic (12.1%) or minimally symptomatic (53%). There was marked variability among surgeons in the use of pre-operative imaging techniques before the initial operation (sestamibi used by 39.4% [26/66] and ultrasound by 39.4% [26/66] also, alone or in combination with other imaging techniques, while 39.4% (26/66) of surgeons used no imaging) and re-exploration.

Conclusions: This survey demonstrates marked variation in pre-operative localisation and surgical management of patients with primary hyperparathyroidism. The majority of surgeons in the UK and Ireland currently perform bilateral neck exploration with or without pre-operative localisation.

Key words: Survey – Primary hyperparathyroidism – Hypercalcaemia – Bilateral neck exploration – Minimally invasive parathyroidectomy – Localisation techniques

Primary hyperparathyroidism (PHPT) is a relatively common endocrine disorder. It is difficult to define the exact incidence of the disease since many patients remain asymptomatic and the reported incidence varies according to the population studied. In the UK, the incidence has been estimated at 25 people per 100,000

population,¹ but it may be as high as 1% in elderly women² or 2.1% in a Swedish population based screening study.³ The diagnosis of PHPT is made following the detection of hypercalcaemia in the presence of elevated, or inappropriately normal, parathyroid hormone (PTH) and the disease is now a different clinical entity from that

Table 1 *Results of the postal survey*

Questions	Possible answers	Results (%)
The majority of patients referred to you are:	Asymptomatic	12.1
	Minimally symptomatic	53.0
	Frankly symptomatic	34.9
In patients with biochemically proven HPT but without symptoms, would you operate?	Always	34.9
	Occasionally or usually	65.2
	Never	0
Which airway device is routinely used?	Endotracheal tube	95.5
	Laryngeal mask	3
	Don't know	1.5
Which incision do you routinely use?	Collar	97
	Lateral approach	3
How do you approach the retrothyroid space?	Via the midline with retraction of strap muscles	95.5
	Between the lateral border of the straps and sternomastoid	4.5
Do you currently perform intra-operative PTH measurements?	Yes	9.1
	No	90.9
Do you currently use intra-operative mapping with a neo-probe?	Yes	4.5
	No	95.5
Do you use intra-operative frozen section?	Routinely	72.7
	Occasionally	16.7
	Never	10.6
Which skin closure do you routinely use?	Staples	37.9
	Sub-cuticular suture	57.6
	Large metal clips	4.5
Do you use drains?	Always	36.4
	Sometimes	46.9
	Never	16.7
Do you routinely measure postoperative calcium?	Yes	100
	No	0
If your answer was 'yes', do you do so?	Daily	65.1
	Day 1 only	16.7
	As an out-patient	10.6
	Other	7.6
Do you routinely manage parathyroid explorations as:	Day-case	1.5
	In-patient	98.5
If as an in-patient, normal length of stay (mean, 2.56 days)	1 day	4.5
	2 days	48.5
	3 days	33.3
	4 days	13.7
Do you routinely prescribe oral calcium supplements?	Yes	9.1
	No	90.9

which was originally described. Many of the patients diagnosed are now classified as minimally symptomatic or asymptomatic although the actual incidence of truly asymptomatic HPT is thought to be quite low.⁴ Hypercalcaemia is usually discovered on routine blood testing, or as part of the investigation of non-specific symptoms of malaise and fatigue. Only rarely now does it present as one of the complications of hyperparathyroidism, the commonest being nephrolithiasis and osteopenia.

Cure can only be affected by surgical excision of the hyper-functioning tissue although research is currently in

progress into the possibility of drugs that are able to inhibit PTH synthesis and secretion.⁵ Drugs are available which reduce hypercalcaemia by inhibiting bone resorption, but this leads to an increase in PTH secretion as abnormal parathyroid tissue does respond to alterations in serum calcium. In recent studies, it has been shown that cardiovascular function, osteoporosis, muscle strength, and neuropsychiatric health improve after parathyroidectomy.⁶⁻¹⁴

During the last decade, several developments have stimulated a change in the traditional approach to para-

thyroid surgery. The advent of more reliable pre-operative imaging techniques, including sestamibi scanning, as well as intra-operative PTH measurement and the use of a hand-held gamma probe and video-endoscopy, have become increasingly popular in the US.¹⁵ In addition, minimally invasive parathyroidectomy has now been described for patients with PHPT, thought to have a single adenoma on pre-operative imaging.¹⁶

In view of these recent advances in pre-operative localisation, intra-operative hormone measurement and surgical technique, this survey was performed to assess the range of management options currently being offered to patients with PHPT in the UK and Ireland.

Methods

In November 2000, a postal questionnaire was sent to all consultant members of the British Association of Endocrine Surgeons (BAES) who live in the UK and Ireland. Responses were anonymous and confidential. Enquiries were made about surgeon characteristics including case-load, indications for surgery, pre-operative localisation performed prior to both primary and secondary explorations, details of operative technique and postoperative management. The questions included in the survey and the responses of the endocrine surgeons are summarised in Table 1 except those related to pre-operative localisation technique performed before the initial operation (Table 2) and re-exploration (Table 3).

Results

Response to the questionnaire

Of the 98 members contacted, 72 replied (73.5%). Six were excluded from further analysis as they were either retired, or no longer performed parathyroid surgery, leaving a response rate from those suitable for analysis of 71.7% (66/92).

Personal characteristics and clinical case-load

The mean age of respondents was 50.6 years (range, 37–70 years), and annual parathyroid caseload 23.1 cases (range, 5–120 cases). The respondents reported that the majority of patients referred to them for surgery were asymptomatic (12.1%, 8/66), minimally symptomatic (53%, 35/66), or frankly symptomatic (34.9%, 23/66). Asked about management of patients with biochemically proven HPT in the perceived absence of symptoms, 34.9% (23/66) would always operate and 65.2% (43/66) do so occasionally or usually. No respondents would adopt a wait-and-see policy in all cases, although influence of patient age was not

Table 2 *Imaging techniques performed before the primary operation*

Imaging techniques	No	%
USS alone	10	15.1
USS + sestamibi	12	18.2
USS + MRI	1	1.5
USS + CT + MRI + sestamibi	1	1.5
USS or none	2	3
MRI + sestamibi	2	3
Sestamibi alone	10	15.1
None	25	37.9
Tc-thallium subtraction	1	1.5
Sestamibi and/or none		1.5

Table 3 *Imaging techniques performed before re-exploration*

Imaging techniques	No	%
USS + CT + MRI + sestamibi	2	3
USS + CT + MRI + sestamibi + PET	1	1.5
USS + CT + sestamibi	4	6.1
USS + CT + sestamibi + selective venous sampling	7	10.6
USS + MRI + sestamibi	3	4.5
USS + MRI + sestamibi + selective venous sampling	4	6.1
USS + sestamibi	5	7.6
USS + sestamibi + selective venous sampling	2	3
CT + MRI + sestamibi	1	1.5
CT + MRI + sestamibi + selective venous sampling	1	1.5
CT + sestamibi	5	7.6
MRI	2	3
MRI + sestamibi	8	12.1
MRI + selective venous sampling	1	1.5
Sestamibi	13	19.7
Sestamibi + selective venous sampling	2	3
Sestamibi + methylene blue	1	1.5
Tc-thallium subtraction scan	1	1.5
None	1	1.5
Selective venous sampling + angiography	1	1.5

enquired after.

Pre-operative localisation

A wide range and combination of localisation techniques are used prior to primary exploration (Table 2). The commonest investigations are sestamibi and ultrasound scanning, both used alone or in combination by 39.4% (26/66) of respondents. A further 39.4% (26/66) routinely do not use pre-operative localisation.

Only one surgeon failed to use pre-operative localisation prior to re-exploration of the neck, with an increased use of investigations by a majority of respondents (Table 3). Sestamibi scanning is routinely requested by 90.9% (60/66), with ultrasound, CT, MRI, and selective venous sampling

also commonly performed. Tc-thallium subtraction scans was used by one respondent, as was angiography, and intra-operative use of methylene blue.

Operative technique

Once anaesthetised, the patient's airway is commonly maintained with an endotracheal tube (95.5%, 63/66). The majority of surgeons perform a collar incision (97%, 64/66) and then approach the retrothyroid space via the midline with lateral retraction of the strap muscles (95.5%, 63/66). Only a small number use a lateral incision (3%, 2/66) with subsequent dissection between the lateral border of the strap muscles and sternomastoid. Intra-operative PTH measurement is performed by only a small proportion of surgeons at present (9.1%, 6/66), with 4.5% (3/66) localising the adenoma intra-operatively with a neo-probe. In contrast, intra-operative frozen-section analysis of excised tissue is still used routinely by 72.7% (48/66) of respondents, and occasionally by a further 16.7% (11/66). Skin is closed by sub-cuticular suture by 57.6% (38/66) of surgeons, staples by 37.9% (25/66), and large metal clips by 4.5% (3/66). Drains are routinely placed by 36.4% (24/66) of respondents, occasionally by a further 46.9% (31/66), whilst 16.7% (11/66) never use a drain.

Postoperative management

All respondents routinely measure postoperative serum calcium levels, 71.2% (47/66) on a daily basis and 21.2% (14/66) on day one only – with subsequent checks on an out-patient basis. One respondent currently manages parathyroid explorations on a day-case basis, the rest as in-patients with mean routine length of stay of 2.56 days (range, 1–4 days). Six (9.1%) of the respondents routinely prescribe oral calcium supplements.

Discussion

The results of this study demonstrate marked variation in the use of pre-operative localisation prior to surgery for primary hyperparathyroidism. Although sestamibi and ultrasound scanning are used alone or in combination by 39.4% of respondents, a further 39.4% routinely use no pre-operative imaging. This may be partly explained by the current surgical approach with the majority of respondents performing bilateral neck exploration (97%) and routine intra-operative frozen section (72.7%).

The debate of bilateral versus unilateral neck exploration continues.^{17,18} For many years, parathyroid surgery has been entirely exploratory, relying on

experienced surgeons to distinguish an adenoma from hyperplasia of all glands. Bilateral neck exploration for PHPT demonstrates cure rates exceeding 95%, with complication rates in the range of 1–2%.^{19,20} In this context, the use of pre-operative imaging may add little benefit and may not be cost effective. Despite these excellent results, surgeons continue to explore new ways to treat patients with PHPT in the hope of improving cosmesis, shortening hospital stay, hastening the return to work, and reducing postoperative pain.²¹

Recently, the need for bilateral neck exploration for all patients with PHPT has been questioned in several studies.^{22,23} If one can accurately localise an adenoma before surgery, then a directed, minimally invasive approach is potentially feasible. Technetium-99m sestamibi scanning, with a sensitivity and specificity of 90% and 98%, respectively, allows unilateral neck exploration for solitary adenomas, with a failure rate of less than 1%.²⁴ The authors of this study concluded that 78% of all patients with sporadic PHPT (90% of the 87% with solitary adenomas) are candidates for unilateral neck exploration. In several studies, the sensitivity of sestamibi scan in PHPT was found to be 80–91%.^{25–30} Recent evidence suggests that the combination of sestamibi scanning and ultrasonography is probably the most accurate parathyroid localisation technique used today, with a reported sensitivity as high as 96%.^{25,31} This technique should allow unilateral, curative surgery in at least 95% of patients, in keeping with current standards produced by the BAES.

Not all pre-operative imaging techniques achieve sensitivity as high as 90% however. Intra-operative quick PTH assay is a recently developed technique that may provide a greater guarantee of surgical cure and can be performed in the operating theatre in approximately 10 min. This, together with accurate pre-operative localisation, has allowed the development of minimally invasive parathyroid surgery.³² A 50% reduction in the serum parathormone level following excision of the adenoma confirms successful removal of all hyper-functioning tissue and precludes the need for further exploration. Minimally invasive surgery is a safe and effective treatment for PHPT. The reduced dissection and decreased operating times associated with this technique allow for more efficient utilisation of theatre time, as well as the possibility of managing these cases on a day-case or short-stay basis.³³ Cure rates for minimally invasive surgery, combined with intra-operative PTH measurement, range from 83–100%.^{16,32,34}

Combined use of sestamibi scanning and a hand-held gamma probe may also improve the success rate of intra-operative localisation,^{35,36} but this is still experimental² with only 3 (4.5%) endocrine surgeons in this study using

a neo-probe for intra-operative mapping. Of respondents, 59 (89.4%) send tissue for frozen-section analysis, either routinely or occasionally, contrasting with a figure of 9.1% for intra-operative quick PTH testing which acts as a 'biochemical frozen section'.³⁷ Only one surgeon currently performs parathyroidectomy as a day-case procedure by a lateral approach, the remaining 65 endocrine surgeons keeping their patients in hospital for a mean of 2.56 days. This survey suggests that parathyroid surgeons in the UK and Ireland do not currently support the move towards minimally invasive parathyroid surgery in Europe and North America.

This study does appear to document a move to earlier surgical intervention in these patients, the majority being minimally symptomatic or asymptomatic. During the last 10 years, surgery has been mainly restricted to patients with complications of the disease following publication of the National Institute of Health³⁸ guidelines in 1990. Recent work, however, suggests that a significant proportion of patients with PHPT are symptomatic, without being aware of this. In a study of 104 patients with no specific symptoms asked to complete the 36-item Short Form Health Survey, initial scores suggested psychosocial disability in a number of domains, with improvement after successful parathyroidectomy.¹¹ The disease can also be progressive in up to 27% of cases,³⁹ with no way of predicting those in whom this will be the case; even in non-progressive disease, surgery still appears to be beneficial. There is, therefore, an increasing body of opinion that surgery should now be offered in all cases unless contra-indicated on grounds of fitness to prevent complications of the disease.^{5,40} There is also evidence that mortality among patients with untreated primary hyperparathyroidism is increased, mainly from cardiovascular disease,⁴¹ although this does appear to be confined to those with the highest calcium concentrations and longest duration of disease and is not affected by parathyroidectomy. It is possible that earlier surgical intervention may reduce the levels of sick leave as well as mortality from this disease.⁴ A recent cross-sectional survey of over 100 members of the American Association of Endocrine Surgeons showed that they also operate on a large number of asymptomatic or minimally symptomatic PHPT patients.⁴² The results of this survey reflect current guidelines for the treatment of PHPT by the BAES that describe a low threshold for surgical intervention.

One of the limitations of this study is that, like other postal questionnaire investigations, the results are based on self-reports and the validity of the data cannot be checked. This survey may also underestimate the practice pattern variation among general surgeons who have less endocrine surgery expertise and perform small numbers of parathyroidectomies each year. In the *Training Requirements and Curriculum for Endocrine Surgery* published by

BAES, surgical trainees are expected to spend one year in a BAES recognised training unit, and perform 10 parathyroid explorations whilst assisting in a further 20. In this survey, the annual case-load of endocrine surgeons is 23.1 operations (range, 5–120 operations) and, as a result, not all units will be suitable for training in parathyroid surgery. This survey does demonstrate, however, marked variation in the pre-operative evaluation and surgical management of PHPT among current members of BAES. Future guidelines may need to allow for the development of minimally invasive techniques if we are to offer our patients the optimal surgical management of this disease.

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