Incremental value and clinical impact of neck sonography for primary hyperparathyroidism: a risk-adjusted analysis

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Background: Despite the different preoperative imaging modalities available for parathyroid adenoma localization, there is currently no uniform consensus on the most appropriate preoperative imaging algorithm that should be routinely followed prior to the surgical management of primary hyperparathyroidism (PHPT). We sought to determine the incremental value of adding neck ultrasonography to scintigraphy-based imaging tests.

Methods: In a single institution, surgically naive patients with PHPT underwent the following localization studies before parathyroidectomy: 1) Tc-99m sestamibi imaging with single photon emission computed tomography/computed tomography (SPECT/CT) or Tc-99m sestamibi imaging with SPECT alone, or 2) ultrasonography in addition to those tests. We retrospectively collected data and performed a multivariate analysis comparing group I (single study) to group II (addition of ultrasonography) and risk of bilateral (BNE) compared with unilateral (UNE) neck exploration.

Results: Our study included 208 patients. Group II had 0.45 times the odds of BNE versus UNE compared with group I (unadjusted odds ratio [OR] 0.45, 95% confidence interval [CI] 0.25–0.81, $p = 0.008$). When adjusting for patient age, sex, preoperative calcium level, use of intraoperative PTH monitoring, preoperative PTH level, adenoma size, and number of abnormal parathyroid glands, Group II had 0.48 times the odds of BNE versus UNE compared with group I (adjusted OR 0.48, 95% CI 0.23–1.03, $p = 0.06$). In a subgroup analysis, only the addition of ultrasonography to SPECT decreased the risk of undergoing BNE compared with SPECT alone (unadjusted OR 0.40, 95% CI 0.19–0.84, $p = 0.015$; adjusted OR 0.38, 95% CI 0.15–0.96, $p = 0.043$).

Conclusion: The addition of ultrasonography to SPECT, but not to SPECT/CT, has incremental value in decreasing the extent of surgery during parathyroidectomy, even after adjusting for multiple confounding factors.

Contexte : Malgré l'existence de diverses modalités d'imagerie préopératoire pour la localisation de l'adénome parathyroïdien, on déplore actuellement l'absence de consensus en ce qui concerne l'algorithme le plus approprié à suivre au chapitre de l'imagerie préalable à une prise en charge chirurgicale de l'hyperparathyroïdie primaire (HPTP). Nous avons voulu vérifier si l'ajout de l'échographie du cou aux tests d'imagerie scintigraphique offrait une valeur ajoutée.

Méthodes : Dans un établissement, des patients atteints d'HPTP n'ayant jamais subi d'intervention chirurgicale ont été soumis à des examens de localisation préparathyroïdectomie : 1) imagerie au moyen du sestamibi marqué au Tc-99m avec tomographie par émission monophotonique/tomodensitométrie (SPECT/CT), ou imagerie au moyen du sestamibi marqué au Tc-99m avec SPECT seule, our 2) échographie en plus de ces tests. Nous avons recueilli les données rétrospectivement et effectué une analyse multivariée pour comparer le Groupe I (examen seul) au Groupe II (ajout de l'échographie) et la probabilité qu'ils subissent une exploration cervicale bilatérale (ECB) plutôt qu'unilatérale (ECU).

Résultats : Notre étude a recruté 208 patients. Le Groupe II s'est trouvé exposé à un risque 0,45 fois plus grand d'être soumis à une ECB plutôt qu'à une ECU, comparativement au Groupe I (rapport des cotes [RC] non ajusté 0,45, intervalle de confiance [IC] de 95 % 0,25–0,81, $p = 0,008$). Après ajustement pour tenir compte de l'âge et du sexe des patients, de leur taux préopératoire de calcium, de la surveillance peropératoire de l'HPT, du taux préopératoire de l'HPT, de la taille de l'adénome et du nombre de ganglions parathyroïdiens anormaux, le Groupe II s'est révélé exposé à un risque 0,48 fois plus grand à l'égard de l'ECB plutôt que de l'ECU comparativement au Groupe I (RC ajusté 0,48, IC de 95 % 0,23–1,03, $p = 0,06$). Selon une analyse de sous-groupe, seul l'ajout de l'échographie à la SPECT a réduit le risque de subir une ECB comparativement à la SPECT seule (RC non ajusté 0,40, IC de 95 % 0,19–0,84, $p = 0,015$; RC ajusté 0,38, IC de 95 % 0,15–0,96, $p = 0,043$).

Conclusion : L'ajout de l'échographie à la SPECT, mais non à la SPECT/CT, a offert une valeur ajoutée pour ce qui est de réduire l'étendue de l'opération durant la parathyroïdectomie, même après ajustement pour tenir compte de plusieurs facteurs de confusion.

Primary hyperparathyroidism (PHPT) is a common endocrine disorder characterized by an elevated parathyroid hormone (PTH) level and hypercalcemia.[1–3] Currently, the most common presentation of PHPT is an asymptomatic individual who is incidentally identified through routine biochemical laboratory testing.[3,4] When PHPT is symptomatic, its most prevalent clinical presentations is nephrolithiasis, followed by musculoskeletal complaints, neuropsychiatric disorders and abdominal symptoms.[1–3] With an incidence of about 1% in the adult population, increasing to 2% in adults aged 55 years and older, PHPT tends to be a disease of middle-aged women.[1,5]

The most common cause of PHPT is a solitary parathyroid adenoma, which accounts for up to 90% of cases.[3,6] Approximately 2% of these adenomas may be found in ectopic locations, including within the mediastinum, carotid sheath or thyroid gland.[3,5] Other causes of PHPT include multiple parathyroid adenomas (5%), 4 gland hyperplasia (5%) and parathyroid carcinoma (< 1%).[1,3,5] Parathyroidectomy is the treatment of choice for PHPT and offers an enduring cure.[1,3,5,6]

Historically, the gold standard approach to parathyroidectomy has been a bilateral neck exploration.[3] However, the advent of increasingly available and accurate preoperative imaging, along with intraoperative PTH measurement, has allowed surgeons to carry out a more focused surgical approach, especially since the vast majority of PHPT cases are caused by a single adenoma.[2,3,7] Combined with other tools, such as the intraoperative parathyroid hormone assay, there has been an increasing number of surgeons advocating for focused parathyroidectomy, such as unilateral neck exploration and minimally invasive parathyroidectomy.[8–14] Moreover, focused parathyroidectomy is associated with decreased surgical dissection and risk of bilateral recurrent laryngeal nerve injury, minimized postoperative pain and shortened length of stay in hospital.[10,15]

Accurate preoperative imaging has facilitated the use of focused parathyroidectomy.[10] Several imaging modalities are available for preoperative localization, including Tc-99m sestamibi imaging (with planar and single photon emission computed tomography; SPECT), neck ultrasonography, and combined Tc-99m sestamibi single photon emission computed tomography with computed tomography (SPECT/CT).[13] Other imaging modalities being studied for parathyroid preoperative localization include magnetic resonance imaging (MRI), positron emission tomography combined with CT (PET/CT), and 4-dimensional angiography-enhanced CT.[16,17]

However, despite the different preoperative imaging tests available for parathyroid adenoma localization, there is currently no uniform consensus on the most appropriate preoperative imaging algorithm that should be routinely followed before the surgical management of PHPT. Moreover, the literature regarding preoperative imaging of PHPT has been primarily focused on the sensitivity and specificity of each imaging test.[1,18] Several studies have examined performance of multiple preoperative imaging tests compared with a single imaging test and have focused their analysis on sensitivity and specificity rather than actual clinical outcomes.[14,19–21] Therefore, the objective of this study was to evaluate whether there is incremental value in adding ultrasonography to a functional imaging test, such as SPECT or SPECT/CT, in reducing the risk of carrying out a bilateral (BNE) versus unilateral (UNE) neck exploration at the time of parathyroidectomy.

Methods

Study hypothesis and objective

We hypothesized that there was an association between preoperative imaging test for localization of parathyroid adenoma in PHPT and extent of surgery. The intervention of interest was the addition of ultrasonography to scintigraphy-based imaging (group II) compared with only scintigraphy-based imaging (group I). The outcome of interest was the relative risk of BNE versus UNE. To account for spurious associations brought on by confounding factors, we used multivariate logistic regression analysis to evaluate this intervention–outcome relationship.

Participants

We retrospectively reviewed all operations carried out for treatment of PHPT between January 2002 and August 2011 at a single Canadian tertiary care centre. St. Paul's

Hospital (Vancouver, BC) is a referral centre for head and neck endocrine surgery, and subspecialty-trained head and neck surgeons performed all operations. There is no formal guideline for preoperative imaging for PHPT at our centre, and there has generally been an even distribution of ultrasonography, SPECT and SPECT/CT for preoperative localization. Frequently, patients undergo either SPECT or SPECT/CT, and some of these patients also undergo ultrasonography of the neck. Our operative approach to PHPT is to begin with a UNE for cases that have localized preoperatively and to proceed with a BNE if a UNE does not identify the adenoma.

For cases that do not localize with preoperative imaging, a BNE is carried out if an adenoma is not on the side of the neck initially explored. Inclusion in the study cohort required the patient to have met diagnostic criteria for PHPT, undergone preoperative localization imaging and undergone neck exploration with pathological confirmation of parathyroid adenoma removal. Individuals who underwent a prior surgical parathyroid exploration and had persistent or recurrent PHPT were excluded. There were 268 cases of PHPT that were reviewed. Nine patients who did not undergo preoperative imaging were excluded. Two patients who did not have an adenoma identified at surgery were also excluded, as were 11 patients who had prior neck explorations. Thirty-eight patients were excluded as they underwent imaging tests in addition to SPECT, SPECT/CT, and/or ultrasonography.

We reviewed patient demographic characteristics, preoperative laboratory studies, imaging findings, operative findings (including intraoperative PTH measurements), extent of operative exploration (UNE v. BNE), adenoma size, postoperative laboratory studies and pathologic diagnoses. We obtained the data by retrospectively reviewing patient charts; imaging, biochemical and pathology results; and operative records. Operative identification of a parathyroid adenoma with pathologic confirmation determined whether a preoperative imaging test resulted in correct preoperative lateralization (left v. right). Cure of PHPT was confirmed by normalization of serum calcium levels within 30 days postoperatively.

Patient information was collected and stored in a deidentified database for data analysis. The study was approved by our institutional review board

Imaging protocols

The protocols for SPECT (comprising planar and SPECT imaging) and SPECT/CT (comprising planar and SPECT/CT imaging) at our centre have been previously described.[18] Imaging of the neck and upper thorax is obtained in the supine position with a low-energy, high-resolution collimator, 10 minutes after intravenous injection of 700 MBq Tc-99m sestamibi. Planar images are obtained over 5 minutes, both immediately and 2 hours postinjection, using a 128-square matrix. Noncircular orbit SPECT is obtained immediately and at 2 hours postinjection using a 128-square matrix with 128 stops, 15 seconds per stop for the early acquisition and 20 seconds per stop for the delayed acquisition. For patients undergoing SPECT/CT, a volumetric CT acquisition is obtained after the delayed SPECT through the same anatomic region (80 kVp, 60 mAs, using CAREDOSE dose modulation). Sets of 1 mm thick contiguous slices are acquired and reconstructed as contiguous 1.25 mm thick slices using a medium-smooth reconstruction kernel. The SPECT/CT images are then generated using iterative reconstruction with 8 subsets and 12 iterations. All imaging was carried out with a Siemens Symbia T6 hybrid SPECT/CT scanner. Finally, the SPECT/CT fused multiplanar images are reviewed on a Siemens Leonardo workstation (Siemens Medical Systems) by a nuclear medicine/radiology dual certified physician.

Statistical analysis

As the outcome of interest was the extent of surgical exploration based on UNE versus BNE, we chose our definition of correct localization based on correct lateralization. We evaluated the proportion of correct lateralization in group I (SPECT v. SPECT/CT) compared with group II (1 of these tests with the addition of ultrasonography) using a Fisher exact test. We used multivariate logistic regression to determine the odds of BNE versus UNE for group I (1 imaging test) compared with group II (addition of ultrasonography to the imaging test). We controlled for the following covariates: age, sex, preoperative calcium, preoperative PTH, use of intraoperative PTH assay, adenoma size (greatest dimension) and number of abnormal parathyroid glands (solitary adenomas v. abnormal parathyroid glands). All data analyses were performed using Stata software version 11.2 (Stata Corp.).

Results

Patients

We reviewed 268 cases of PHPT. Nine patients who did not undergo preoperative imaging were excluded. Two patients who did not have an adenoma identified at surgery were also excluded, as were 11 patients who had prior neck explorations. We excluded a further 38 patients because they underwent imaging tests in addition to SPECT, SPECT/CT and/or ultrasonography. Our final cohort consisted of 208 patients who had undergone SPECT, SPECT/CT or the addition of ultrasonography to these tests preoperatively.

The clinical and pathological characteristics of patients are summarized in Table 1. There were 156 (75.0%) women and 52 (25.0%) men. The mean age was 58.6 ±

13.6 years. There were 8 (3.8%) cases of multiglandular disease (5 double adenomas and 3 sporadic 4-gland hyperplasias) and 2 (1.0%) cases of parathyroid carcinoma. Ectopic adenomas accounted for 7 (3.4%) cases, and all were solitary. Excluding the parathyroid carcinomas and ectopic adenomas, there were 191 (91.8%) cases with a pathological diagnosis of solitary parathyroid adenoma. The mean patient follow-up, as defined by the date of the last serum calcium measurement, was 140 days.

Baseline preoperative laboratory data were collected and all patients underwent biochemical testing postoperatively. Ionized calcium levels were corrected for the patients' blood pH. The preoperative calcium levels were 2.75 ± 0.19 mmol/L for total calcium level (reference range 2.18–2.58 mmol/L) and 1.52 ± 0.13 mmol/L for ionized calcium level (reference range 1.17–1.29 mmol/L). Postoperative follow-up calcium levels were 2.33 ± 0.17 mmol/L for total calcium level and 1.26 ± 0.09 mmol/L for ionized calcium level.

The majority of study patients (67.4%) underwent parathyroidectomy with intraoperative parathyroid hormone measurement during which a 50% drop at 5 or 10 minutes after adenoma removal, from baseline or pre-excision levels, was considered predictive of cure. Baseline PTH measurements were 19.8 ± 25.9 pmol/L (reference range 1.3–6.8 pmol/L). Intraoperative PTH measurements were 22.9 ± 20.5 pmol/L, 19.0 ± 20.9 pmol/L, 8.5 ± 8.9 pmol/L and 6.3 ± 6.4 pmol/L for baseline pre-excision at 0 minutes, 5 minutes and 10 minutes after adenoma resection, respectively.

Correct localization by imaging tests

We evaluated the incremental value of ultrasonography with respect to proportion of correct localization in patients who underwent only 1 preoperative imaging test (group I) versus patients who had the addition of ultrasonography to a preoperative imaging test (group II). There were 75 patients in group I and 133 patients in group II. Group II had 78.9% correctly localized parathyroid adenomas compared with only 54.7% in group I ($p < 0.001$). In a subgroup analysis, the addition of ultrasonography to SPECT improved correct localization from 45.9% to 75.8% ($p < 0.001$). The addition of ultrasonography to SPECT/CT, however, did not significantly improve correct preoperative localization ($p = 0.30$; Table 2).

Impact of preoperative imaging test on extent of surgery

We assessed the clinical impact of adding ultrasonography to a preoperative imaging test using logistic regression models evaluating the odds of BNE versus UNE during parathyroidectomy. These results are summarized in Table 3. Univariate analyses are illustrated as unadjusted

Table 1. Descriptive statistics for unilateral (UNE) versus bilateral (BNE) neck exploration

	Group; mean ± SD or no. (%)*			
Factor	Overall, *n* = 208	UNE, *n* = 138	BNE, *n* = 70	*p* value†
Age, yr	58.6 ± 13.5	59.3 ± 14.2	57.1 ± 12.2	0.26
Sex, female	156 (75.0)	103 (74.6)	53 (74.7)	0.87
Preoperative Ca, mmol/L	2.75 ± 0.19	2.76 ± 0.18	2.73 ± 0.19	0.19
Intraoperative PTH assay	139 (66.8)	101 (73.2)	38 (54.3)	0.006
PTH, nmol/L	19.8 ± 25.9	22.6 ± 28.9	14.4 ± 17.5	0.032
Greatest dimension, cm	1.76 ± 1.02	1.91 ± 1.17	1.50 ± 0.61	0.011
Adenoma type				0.002
Solitary	191 (91.8)	133 (96.3)	58 (82.9)	—
Double	5 (2.4)	0 (0)	5 (7.1)	—
Ectopic	7 (3.4)	4 (3.0)	3 (4.3)	—
Hyperplasia	3 (1.4)	0 (0)	3 (4.3)	—
Carcinoma	2 (1.0)	1 (0.7)	1 (1.4)	—
Imaging studies				0.007
Group I	75 (36.0)	41 (29.7)	34 (48.6)	—
SPECT only	61 (29.3)	28 (20.3)	33 (47.2)	—
SPECT/CT	14 (6.7)	13 (9.4)	1 (1.4)	—
Group II	133 (64.0)	97 (70.3)	36 (51.4)	—
SPECT+ ultrasonography	62 (29.8)	42 (30.4)	20 (28.6)	—
SPECT/CT+ ultrasonography	71 (34.1)	55 (39.9)	16 (22.8)	—

BNE = bilateral neck exploration; Ca = calcium; CT = computed tomography; PTH = parathyroid hormone; SD = standard deviation; SPECT = single photon emission computed tomography; UNE = unilateral neck exploration.
*Unless otherwise indicated.
†The *p* value for differences between UNE and BNE was calculated using a 2-sided *t* test (continuous data) and χ^2 test (categorical data).

odds ratios (ORs) with associated 95% confidence intervals (CIs) and p values for association. Parallel representation is demonstrated for multivariate analyses, which have been adjusted for the following confounders: age, sex, preoperative serum calcium, intraoperative PTH assay, preoperative PTH levels, size of adenoma and number of abnormal parathyroid glands (solitary v. multiple).

Group II had 0.45 times the odds of BNE versus UNE compared with group I (unadjusted OR 0.45, 95% CI 0.25–0.81, p = 0.008). The adjusted analysis demonstrates that group II had 0.48 times the odds of BNE versus UNE compared with group I (adjusted OR 0.48, 95% CI 0.23–1.03, p = 0.06). We performed a subgroup analysis to determine the incremental value of ultrasonography to SPECT and to SPECT/CT. Adding ultrasonography to SPECT for preoperative imaging of PHPT reduces the odds of BNE by 62% compared with SPECT alone (adjusted OR 0.38, 95% CI 0.15–0.96, p = 0.043). However, the addition of ultrasonography to SPECT/CT for preoperative localization of PHPT does not reduce the odds of undergoing BNE compared with SPECT/CT alone (adjusted OR 2.93, 95% CI 0.18–46.5, p = 0.31).

Discussion

The present study evaluates the incremental value of untrasonography on preoperative parathyroid adenoma localization tests in terms of correct lateralization and clinical impact on extent of parathyroid surgery (BNE v. UNE). The overall results suggest that there is incremental value in adding ultrasonography to an imaging test to localize a parathyroid adenoma preoperatively, as well as to reduce the risk of BNE and the extent of operative neck exploration. Interestingly, a subgroup analysis demonstrated that ultrasonography provides added value in correctly localizing a parathyroid adenoma preoperatively and reduces the chance of BNE when combined with SPECT but not when combined with SPECT/CT.

Other studies have also reported incremental value when combining preoperative localization studies. Purcell and colleagues[14] evaluated ultrasonography and planar scintigraphy (conventional 2-dimensional imaging without SPECT) for parathyroid localization and found that their sensitivity was 57% and 54% for the tests, respectively, but that combining the tests increased the sensitivity to 78%. In a prospective clinical study, the combination of ultrasonography and planar scintigraphy had 96% sensitivity, 83% specificity, 88% positive predictive value and 94% negative predictive value.[19] A recent review by Johnson and colleagues[20] also concluded that preoperative PHPT patient imaging with ultrasonography and planar scintigraphy most accurately predicted the location of solitary adenomas when compared with either imaging test alone. These findings are consistent with the results of the present study, although our study further validated the value added of combining ultrasonography and planar imaging with either SPECT or SPECT/CT scintigraphy by evaluating the impact on the extent of parathyroid exploration.

The protection against BNE afforded by ultrasonography is supported by reports of surgeon-performed ultrasonography for preoperative parathyroid adenoma localization.[22–24] These studies underscore the importance of operator experience for clinically informative neck ultrasonography and suggest that the selective addition of sestamibi imaging (for cases in which the ultrasound was negative or equivocal) is the most cost-effective preoperative approach and the most protective against BNE.[22,23,25] Our results echo the utility of ultrasonography in preoperative imaging for PHPT, especially for imaging modalities that alone may not adequately facilitate a focused neck exploration.

A retrospective case series recently evaluated the incremental value of combining ultrasonography and SPECT/CT with software fusion for preoperative localization of parathyroid adenomas.[21] Fifty-nine patients were evaluated in this study, and the sensitivity of ultrasonography and SPECT/CT was 64% and 90%, respectively, with concordant

Table 2. Degree of correct lateralization, by imaging test

Imaging test	No. (%)
Group I, n = 75	41 (55)
SPECT only, n = 61	28 (46)
SPECT/CT, n = 14	13 (93)
Group II, n = 133	105 (79)
SPECT + ultrasonography, n = 62	47 (76)
SPECT/CT + ultrasonography, n = 71	58 (82)

CT = computed tomography; SPECT = single photon emission computed tomography.

Table 3. Odds of bilateral versus unilateral neck exploration

Model*	OR (95% CI)	p value
Group I v. group II		
Group I	0.45 (0.25–0.81)	0.008
Group II	0.48 (0.23–1.03)	0.06
SPECT v. SPECT + ultrasonography		
SPECT	0.40 (0.19–0.84)	0.015
SPECT + ultrasonography	0.38 (0.15–0.96)	0.043
SPECT/CT v. SPECT/CT + ultrasonography		
SPECT/CT	3.78 (0.46-31.1)	0.22
SPECT/CT + ultrasonography	2.93 (0.18-46.5)	0.31

CI = confidence interval; CT = computed tomography; OR = odds ratio; SPECT = single photon emission computed tomography.
*Model adjusted for age, sex, preoperative calcium, intraoperative parathyroid hormone (PTH) monitoring, preoperative PTH level, size of adenoma, and type of adenoma (solitary v. nonsolitary).

ultrasonography and SPECT/CT findings in 59% of cases.[21] The observation that combined ultrasonography and SPECT/CT had an overall sensitivity of 95% and accuracy of 91% led this group to conclude that there was incremental value in combining these tests for preoperative localization.[21] Our findings are not entirely consistent with this group's observations, as we did not observe any significantly increased value added in combining SPECT/CT with ultrasonography. A potential reason for this difference might be the fairly high rate at which SPECT/CT was able to correctly localize a parathyroid adenoma preoperatively (92.8%).

The risk of ionizing radiation from SPECT/CT must be considered. A recent study quantified the radiation exposure associated with SPECT/CT of the neck and postulated that it would take anywhere from 2390 to 8030 scans to cause 1 case of radiation-induced cancer, depending on patient age and sex.[26] Thus, the most appropriate role for SPECT/CT may be as part of the preoperative evaluation of complex PHPT. Several recent studies have supported SPECT/CT as a valuable preoperative imaging modality for PHPT, particularly in cases of multi-glandular disease and ectopic parathyroid adenoma.[5] Case series have suggested promise for this technique as an evolving method of preoperative localization for PHPT.[18,27] Our results are consistent with these findings.

Despite the value in combining preoperative imaging studies, there is also evidence to support the use of a single preoperative imaging test. Moure and colleagues[11] evaluated the utility of planar scintigraphy alone in localizing parathyroid adenomas and guiding UNE. The results of their study suggested that patients with PHPT and unequivocally positive planar scintigraphy scans may safely undergo a focused parathyroidectomy without additional preoperative imaging.[11] In contrast, our results suggest that by adding ultrasonography to SPECT, there is an increased probability of accurate preoperative parathyroid localization, and we have demonstrated that this will lead to decreased extent of neck exploration during parathyroidectomy.

While several outcomes (e.g., cure of PHPT) could have been evaluated, we specifically chose extent of parathyroid surgery. This is an important outcome to evaluate, as it is clinically relevant for both surgeons and patients, does not depend on complete 1-year follow-up and is not subject to censoring of data as a result of cases being lost to follow-up.

One of the strengths of the present study is our 100% complete data on the primary outcome of interest. Perhaps the most important contribution of the present report is translating the impact of preoperative imaging tests on clinically relevant outcomes, specifically the extent of parathyroid surgery that must be carried out for a successful parathyroidectomy. Our results suggest that combining SPECT with ultrasonography is a safe and informative preoperative imaging practice for PHPT that reduces the risk of BNE and helps facilitate a focused parathyroid operation.

Limitations

The present study has several limitations. Two are its relatively small sample size and its retrospective nature. The retrospective nature of our study did not allow for implementation of a standardized protocol for preoperative imaging in PHPT. We attempted to account for this type of bias by incorporating the type of imaging test ordered into our multivariate model and the effect on extent of surgery. While this approach is reasonable in most instances, we had a relatively small sample size (n = 208) with only 70 outcomes of interest (BNE). Given the number of covariates in our multivariate analysis, our adjusted model may be susceptible to being overfitted. We also did not validate our model, as we could not stably model our outcome of interest by splitting our database into test and validation subsets.

Conclusion

We examined the clinical utility of adding ultrasonography to 2 commonly performed preoperative imaging investigations for PHPT — SPECT and SPECT/CT — assessed on the basis of accuracy of preoperative localization and the extent of surgical exploration subsequently required. Our analysis demonstrates that greater incremental value is gained by adding ultrasonography to SPECT rather than to SPECT/CT. Further study of techniques for accurately localizing abnormal parathyroid glands preoperatively, particularly in a prospective or randomized controlled study design, is an important future direction that will ultimately lead to improved outcomes for individuals with PHPT.

Competing interests: None declared.

Contributors: M.C. Tee, D.S. Levine and S.M. Wiseman designed the study. M.C. Tee, V. Nguyen, S.S. Strugnell, J. Yang, P. Tiwari, D.S. Levine and S.M. Wiseman acquired the data, which M.C. Tee, S.K. Chan, S. Jones and S.M. Wiseman analyzed. M.C. Tee, V. Nguyen and S.M. Wiseman wrote the article, which M.C. Tee, S.K. Chan, S.S. Strugnell, S. Jones, P. Tiwari, D.S. Levine and S.M. Wiseman reviews. All authors approved the article for publication.

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