Diagnostic Imaging Pathways - Hyperparathyroidism (Primary Suspected)

Population Covered By The Guidance

This pathway provides guidance on the imaging of adult patients with suspected hyperparathyroidism.

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Quick User Guide

Move the mouse cursor over the PINK text boxes inside the flow chart to bring up a pop up box with salient points. Clicking on the PINK text box will bring up the full text. The relative radiation level (RRL) of each imaging investigation is displayed in the pop up box.

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Pathway Diagram
INVESTIGATION OF PRIMARY HYPERPARATHYROIDISM

Is unilateral parathyroid or minimally invasive surgery being considered?

No

Bilateral neck surgical exploration ± intraoperative US

Yes

Sestamibi Scan ± Subtraction 99mTc-Pertechnetate Scan

Ultrasound of the neck

In selected patients, consider 4D CT, 18F-Fluorocholine PET-CT or selective venous sampling

Surgery

Recurrent hyperparathyroidism

- Seek Endocrinology Opinion
- Reconfirm hyperparathyroidism
- Review indications for repeat surgery

Sestamibi Scan ± Subtraction 99mTc-Pertechnetate Scan

Sestamibi positive in chest?

No

Both US and Sestamibi negative

Consider 4D CT or selective venous sampling

Yes

US or Sestamibi positive in neck

4DCT

Surgery
Parathyroid Adenoma

Image 1 (Ultrasound): A well circumscribed hypoechoic mass measuring up to 8mm is located deep to the inferior left thyroid pole. The appearances are consistent with a parathyroid adenoma.

Parathyroid Adenoma

Image 2a, 2b (Pertechnetate and Sestamibi Study), and 2c (SPECT): Initial pertechnetate images show uniform tracer distribution throughout both thyroid lobes apart from a small focal area of increased tracer uptake at the inferior pole of the left lobe of the thyroid gland.

MIBI early and delayed images show increased uptake in the left and right lower poles of the thyroid. On subtraction images, there is an area of increased tracer activity near the inferior pole of the left lobe of the thyroid gland which represents abnormal parathyroid tissue (arrow).

SPECT is used to help anatomically define the abnormal area.

Parathyroid Adenoma

Image 3 (H&E, x2.5): Histological section of a parathyroid adenoma showing sheets of monotonous oncocytic cells (blue arrows) and chief cells (green arrows) with no adipose tissue.

Teaching Points

- Imaging for preoperative localisation of the parathyroid glands remains controversial although it is generally recommended for minimally invasive or unilateral neck surgery
- Understanding the accuracy of each modality is vital in selecting the most appropriate preoperative imaging technique
- Ultrasound and Sestamibi scans are sensitive methods used as first line investigations, frequently in combination
- 4DCT has the advantage of superior anatomical localisation but is usually reserved for equivocal or
negative ultrasound and nuclear medicine studies
- Preoperative imaging is required for recurrent or persistent hyperparathyroidism to minimise the risks of repeat surgery and to maximise the chances of successful treatment

Primary Hyperparathyroidism

- Primary hyperparathyroidism is an endocrine disorder resulting from the autonomous functioning of one or more parathyroid glands 1,2
- The causes of primary hyperparathyroidism include a single parathyroid adenoma (80-85%), parathyroid hyperplasia (10-15%), multiple adenomas (2-3%), and very rarely, parathyroid adenocarcinoma (95% in experienced hands). Therefore, pre-operative localisation studies were not usually necessary 3
- Increasingly, surgeons prefer preoperative imaging, especially when considering minimally invasive surgery 1,3,4
- Imaging is usually required when there is recurrent disease as the success rates for repeat bilateral neck exploration after an initial failed surgery may be as low as 60%. In such cases of recurrent or persistent hyperparathyroidism, localisation studies have improved the ability to identify the site of the remaining abnormal parathyroid tissue 2,5
- The main advantages of preoperative imaging are 6,7
  - The potential to reduce the time in surgery
  - The ability to limit surgical exploration to the affected side
  - The detection of ectopic abnormal parathyroid glands
- Technetium Tc-99m sestamibi imaging and sonography have been the most widely used imaging techniques for the localisation of parathyroid adenomas 1
- Invasive procedures such as selective venous sampling and selective angiography are expensive and technically difficult and therefore rarely used
- Image-guided biopsy is performed in cases where percutaneous ethanol ablation as a first line therapy is considered or when the results of imaging procedures are equivocal 8
- Note: It is important to consider and exclude Familial Hypocalciuric Hypercalcaemia (FHH) in mild cases of primary hyperparathyroidism. FHH does not require surgery and is a major cause of "failed" neck exploration in primary hyperparathyroidism

Intraoperative Ultrasound

- May be useful in difficult cases and may limit the extent of dissection in a previously operated field 8
- Inexpensive, non-invasive and reproducible option in the operating room if expert sonographers available 9

Sestamibi Nuclear Medicine Scan and Subtraction Pertechnetate Scan

- Used for preoperative localisation of abnormal parathyroid glands in the following cases
  - Where minimally invasive surgery is intended 10
  - Recurrent or persistent hyperparathyroidism 5,11
  - Difficult cases 12
- Includes the neck and the mediastinum for detection of ectopic abnormal parathyroid glands
- High sensitivity (50-75%) and specificity (>90%) for the detection of abnormal parathyroid glands
Correlating the functional imaging provided by sestamibi scan with a technique with superior anatomical resolution such as SPECT, SPECT-CT, US or 4DCT improves the sensitivity for detection of abnormal parathyroid tissue. Sestamibi accumulates in both parathyroid tissue and thyroid nodules and anatomical localisation of the abnormality is based on washout properties.

99mTc-pertechnetate is a thyroid selective radioisotope that can be used in combination with sestamibi. It is especially useful in patients with suspected or known thyroid disease or previous thyroid surgery. Digital subtraction methods can be used as an aid in identifying sestamibi accumulation due to abnormal parathyroid tissue.

**Limitations**
- Relatively poor image resolution and anatomical information (compared to US or CT)
- False negatives can occur in patients with small adenomas and with hyperplasia

**Ultrasound**
- Used for identification and localisation of parathyroid adenomas in patients with primary hyperparathyroidism who undergo minimally invasive surgery.
- Its sensitivity for detecting parathyroid neoplasms ranges between 36% to 78%. In view of this, many authors now propose the use of ultrasound in combination with another imaging modality, most commonly scintigraphy.

**Advantages**
- Superior anatomical resolution (provides more detailed information of adenoma characteristics and relationships to other structures in the neck)
- Useful in evaluation of thyroid abnormalities
- Relatively inexpensive
- Does not emit ionising radiation

**Limitations**
- Inability to localise the small percentage (2%) of parathyroid adenomas, particularly intrathyroidal, deeply located and ectopic mediastinal lesions
- Low sensitivity in recurrent or persistent primary hyperparathyroidism
- Operator dependent and subjective

**18F-Fluorocholine PET-CT**
- 18F-Fluorocholine PET-CT provides both anatomical and physiological information.
- Although there is a lack of high-grade evidence regarding 18F-fluorocholine PET-CT for hyperparathyroidism, pilot studies have demonstrated a sensitivity and specificity of 92% and 100% respectively.

**Persistent or Recurrent Hyperparathyroidism**
- The incidence of persistent or recurrent disease following surgery for hyperparathyroidism is 5-10%.
- Multiple potential causes could lead to recurrent disease including but not limited to inadequate excision, a second adenoma, multigland hyperplasia or hyperactive ectopic parathyroid tissue.
- In such cases, the diagnosis of primary hyperparathyroidism should be re-confirmed and the
indications for surgery should be reviewed.  

- Preoperative localisation is required in patients being considered for repeat surgery to more precisely define the site of abnormal parathyroid tissue and to minimise the risks associated with repeat surgery due to fibrosis.
- Preoperative localisation improves the success rate from 60% to more than 95%.
- It is still debated which combination of imaging modalities represents the optimum assessment. However, most agree that at least two modalities should be performed, one of which should be a sestamibi scan.

### Four-dimensional computed tomography (4DCT)

- CT of the neck and mediastinum is generally considered second line investigation in the assessment of primary hyperparathyroidism, following on from equivocal or negative ultrasound or nuclear medicine studies.
- The main advantage is superior spatial resolution and the detailed anatomical localisation of ectopic mediastinal lesions for surgical planning.
- The sensitivity of CT for preoperative localisation of abnormal parathyroid tissue ranges from 78% to 92%.
- Four-dimensional computed tomography involves acquisition of CT images during two or more contrast enhancement phases usually non-contrast, arterial and delayed phase.
- 4DCT is able to provide detailed anatomical and functional information.
- Several recent studies have shown 4DCT to be more sensitive than US and 99m Tc-MIBI scanning for localizing parathyroid tissue.
- Currently 4DCT is more widely accepted as a second-line investigation or in patients undergoing repeat surgery.
- Benefits include the speed and simplicity in image acquisition while limitations to consider include:
  - Exposure to ionising radiation
  - The use of intravenous contrast

### Selective Venous Sampling

- Selective venous sampling is an invasive procedure which is generally only considered in the preoperative localisation of abnormal parathyroid tissue for recurrent or persistent hyperparathyroidism when non-invasive imaging methods have failed.
- It involves selective cannulation of cervical and mediastinal veins to sample venous PTH levels. Local elevations of serum PTH compared to peripheral levels allow target areas to be defined for surgery (at least a two-fold gradient is required). Therefore, the effectiveness of this procedure depends upon production of PTH by the parathyroid glands and not on their size.
- In the setting of recurrent or persistent hyperparathyroidism, the sensitivity for the localisation of abnormal parathyroid tissue ranges from 80 to 94% and the specificity from 85 to 100%.
- The disadvantages of selective venous sampling include:
  - Invasiveness with risks of haemorrhage and infection
  - Exposure to ionising radiation and intravenous contrast
  - Inability to direct the surgeon to an exact anatomical location

### References
References are graded from Level I to V according to the Oxford Centre for Evidence-Based Medicine, Levels of Evidence. Download the document

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