Norfolk and Norwich University Hospitals NHS Foundation Trust

James Paget University Hospitals NHS Foundation Trust

Part of East Anglia Thyroid Cancer Multi-Disciplinary Team

Joint Trust Guideline for the Management of Thyroid Nodules in Adults

A clinical guideline recommended

For use in:	Endocrinology, General Medicine, Endocrine Surgery, ENT, Oncology, Radiology, Nuclear Medicine
By:	Consultants and junior staff
For:	Adult patients with thyroid nodules
Division responsible for document:	Medical Division
Key words:	Thyroid, Nodules
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Compliance links: *(is there any NICE related to guidance)*	No NICE
If Yes - does the strategy/policy deviate from the recommendations of NICE? If so why?	N/a

This guideline has been approved by the Trust's Clinical Guidelines Assessment Panel as an aid to the diagnosis and management of relevant patients and clinical circumstances. Not every patient or situation fits neatly into a standard guideline scenario and the guideline must be interpreted and applied in practice in the light of prevailing clinical circumstances, the diagnostic and treatment options available and the professional judgement, knowledge and expertise of relevant clinicians. It is advised that the rationale for any departure from relevant guidance should be documented in the patient's case notes.

The Trust's guidelines are made publicly available as part of the collective endeavour to continuously improve the quality of healthcare through sharing medical experience and knowledge. The Trust accepts no responsibility for any misunderstanding or misapplication of this document**.**

Version and Document Control:

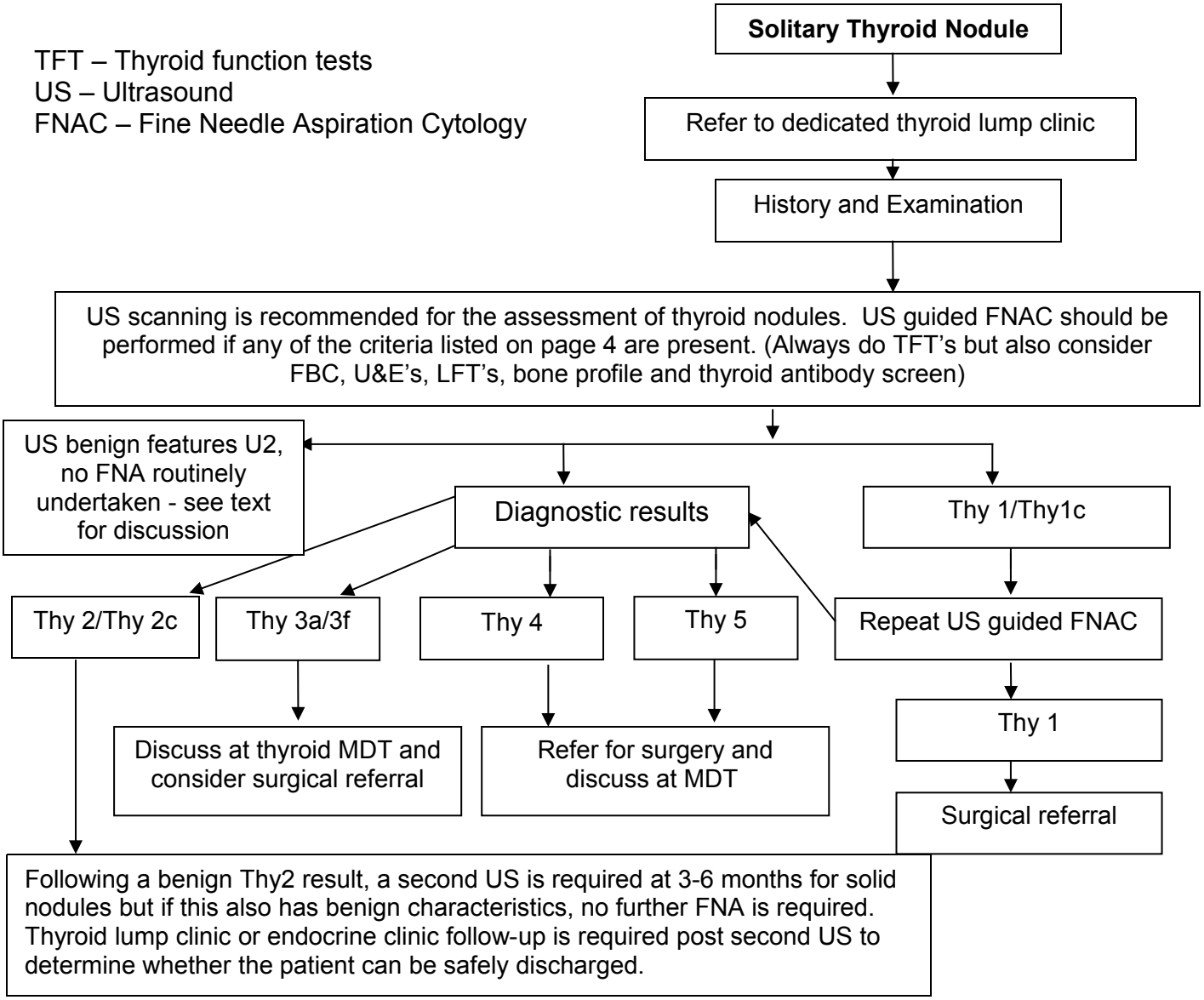
Version Number	Date of Update	Change Description	Author
2	08/08/2017	Include what to do with PET positive nodules, and to incorporate some minor changes from the UK National Guidelines on Thyroid Cancer, and the US guidelines on Thyroid Nodules And Thyroid Cancer Particularly around a New Imaging Classification.	Dr Ketan Dhatariya Dr Frankie Swords
2.1	19/05/2020	No clinical changes. Trust template updated.	Dr Ketan Dhatariya
2.2	28/07/2020	Reviewed. No clinical changes.	Dr Ketan Dhatariya

This is a Controlled Document

Printed copies of this document may not be up to date. Please check the hospital intranet for the latest version and destroy all previous versions.

Quick reference guideline/s

TFT – Thyroid function tests
US – Ultrasound
FNAC – Fine Needle Aspiration Cytology



Thy 1/ Thy 1c ---Non diagnostic or inadequate for cytological purposes. c = cyst fluid only

Thy 2/ Thy 2c ---Non-neoplastic (consistent with nodular goitre or thyroiditis), or non-neoplastic cystic lesion

Thy 3a ----------Cytological atypia or other features which raise the possibility of neoplasia, but which are insufficient to enable confident placing into any other category

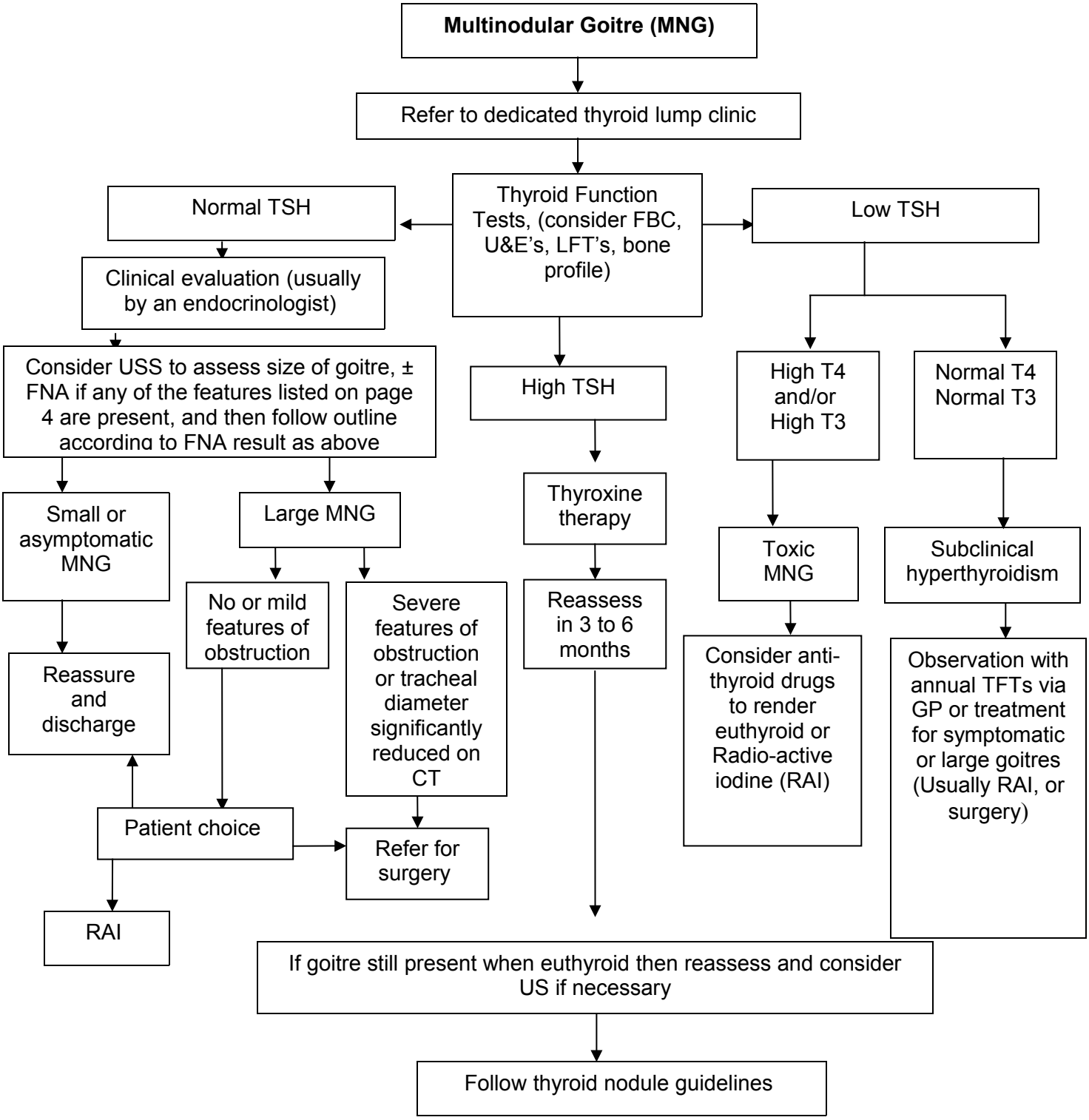
Thy 3f ----------All follicular lesions, or samples consisting almost exclusively/exclusively of Hürthle cells

Thy 4 ----------Samples which are suspicious of malignancy, but which do not allow confident diagnosis of malignancy

Thy 5 ----------Samples are those that can be confidently diagnosed as malignant.

All lesions classified as Thy 3, 4 or 5 should be discussed at the next thyroid cancer multi-disciplinary team meeting

Joint Trust Guideline for the Management of Thyroid Nodules in Adults



All lesions classified as Thy 3, 4 or 5 should be discussed at the next thyroid cancer multi-disciplinary team meeting

Guidelines for US staging and FNA of thyroid nodules

The ultrasound "U" classification of thyroid nodules has been developed by the British Thyroid Association as part of their 2014 guidelines on the management of thyroid cancer. It allows for stratifying thyroid nodules as benign, suspicious or malignant based on ultrasound appearances termed U1-U5.

Classification

U1 (normal)

no nodules

U2 (benign)

hyperechoic or isoechoic with a halo

cystic change with ring down artefact (colloid)

microcystic or spongiform appearance

peripheral egg-shell calcification

peripheral vascularity

U3 (indeterminate)

solid homogenous markedly hyperechoic nodule with halo (follicular lesions)

hypoechoic with equivocal echogenic foci or cystic change

mixed or central vascularity

U4 (suspicious)

solid hypoechoic (compared with thyroid)

solid very hypoechoic (compared with strap muscles)

hypoechoic with disrupted peripheral calcification

lobulated outline

U5 (malignant)

solid hypoechoic with a lobulated or irregular outline and microcalcification

papillary carcinoma

solid hypoechoic with a lobulated or irregular outline and globular calcification

medullary carcinoma

intranodular vascularity

taller than wide axially (AP > TR)

characteristic associated lymphadenopathy

US appearances that are indicative of benign nodules (U1-2) should be regarded as reassuring. No need to perform an FNA UNLESS the patient has a statistically high risk of malignancy.

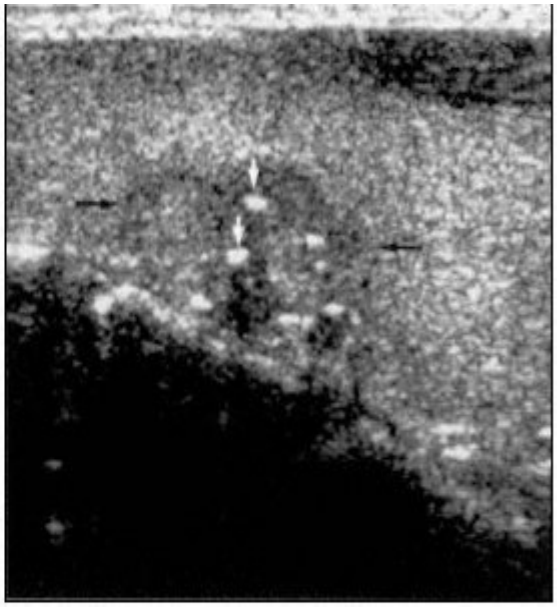
US appearances that are equivocal, indeterminate or suspicious of malignancy (U3-5), should always prompt an US guided FNAC.

Nodules with Thy2 cytology but indeterminate or suspicious US features should undergo repeat FNAC for confirmation.

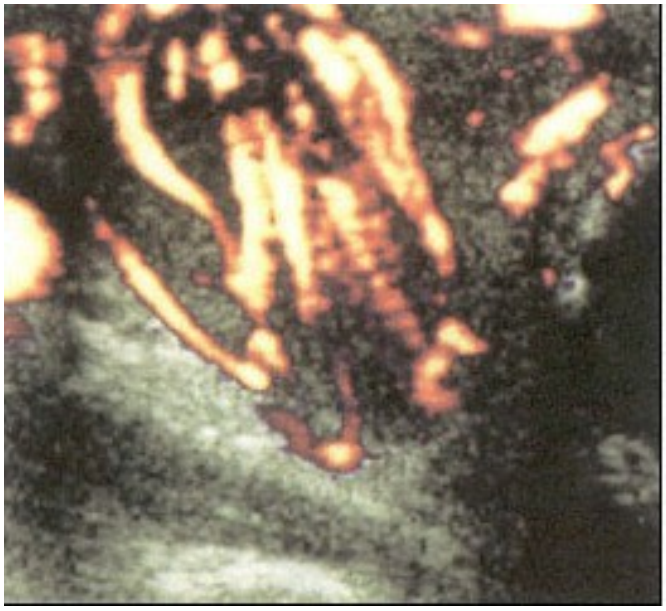
Nodules detected by PET-CT with focal FDG activity should be investigated with ultrasound and FNAC.

FNA if:

1) There is a history of rapid enlargement (suggests lymphoma/anaplastic thyroid cancer)
2) There is slow but progressive growth – suggests malignant involvement
3) There is punctate calcification on ultrasound- suggestive of papillary thyroid cancer (see examples below)



4) There is invasion of other structures i.e. oesophagus, trachea or strap muscles, or pathological lymphadenopathy
5) Solid hypoechoic nodules > 1cm
6) There is type III vascularity (striking intranodular flow on doppler) – see image below



Type III vascularity

Consider FNA if there is a

1) Family history of papillary thyroid cancer, medullary thyroid cancer or MEN2 in first degree relatives
2) Previous history of neck irradiation

AVOID FNA in the following cases:

1) Thyrotoxic patients (malignancy is very uncommon in an autonomous nodule/toxic gland
2) Patients presenting with acute pain and tenderness (suggests haemorrhage into a nodule)
3) Multinodular goitre (unless there are suspicious features as described in the previous section) There is no need to FNA the dominant nodule if there are no worrying features
4) Comet tail or ring calcification on ultrasound

Comet tail artefact

Ring calcification

5) Spongiform isoechoic nodules or purely cystic lesions

Spongiform isoechoic nodule

Objective/s

These guidelines have been developed to ensure that there is consistency in diagnosis and management amongst the different specialities to which thyroid nodules may present.

Rationale

These guidelines aim to provide a rational algorithm to ensure that nodules can be quickly and appropriately managed without unnecessary over-investigation, whilst minimising the risk of missing a thyroid malignancy (see pages 2 and 3).

Broad recommendations

- **All patients with a thyroid lump should be seen in a dedicated thyroid lump clinic – this should be the first point of contact upon referral to hospital.**
- All patients require a history and examination, and thyroid function tests (to include TSH and fT4 and fT3 where indicated) prior to ultrasound scanning.
- **Ultrasound scanning is the first line recommended investigation of a thyroid nodule.**

Background

A thyroid nodule is a discrete lesion within the thyroid gland that is palpably and / or ultrasonographically distinct from the surrounding thyroid parenchyma. Palpable thyroid nodules are very common, being present in approximately 4 to 8% of the population. The prevalence of nodules found at post mortem examination, during surgery or by ultrasound approaches 70%. Up to 35% of thyroid glands removed at post mortem or at surgery, contain clinically unimportant (i.e. < 1.0 cm) papillary carcinomas.

The incidence of nodules rises with age with a lifetime risk of 5 to 10% of developing a palpable thyroid nodule. About 50% of nodules are solitary, with another 25% being the dominant nodule within a multinodular goitre. Nodules may be filled with either colloid or fluid. They may be neoplastic or inflammatory. Women are 4 times more likely to develop solitary nodules than men. Incidence also increases in areas of iodine deficiency. Whilst the fear amongst patients is that a thyroid lump may be malignant, the results of several case series looking at the results of Fine Needle Aspiration Cytology (FNAC) have shown that approximately 70% of nodules biopsied were benign, 25% were indeterminate or suspicious, and only 5% were definitely malignant. The risk of malignancy is the same for palpable or non-palpable nodules (i.e. picked up on US scanning only).

The natural history of thyroid nodules is such that with no intervention, up to 35% may disappear on their own.

Approximately 15 to 25 % of all nodules are either purely cystic or complex (i.e. partly cystic and partly solid). On aspiration, the presence of blood in the fluid is NOT an indicator of malignant potential.

Nodules found during pregnancy should follow the normal algorithm. Surgery, when necessary, should be delayed until the 2nd trimester.

Management

Clinicians should be *highly* suspicious of thyroid cancer if the patient presents with any of the following:

a) If there is a personal or family history of medullary thyroid cancer, multiple endocrine neoplasia (in which case measure a calcitonin level), or familial polyposis.
b) Rapid growth of the lump.
c) Age of either < 20 or > 70 years old.
d) An irregular nodule that may be very firm or hard.
e) Nodule ‘fixed’ to underlying anatomical structures.

f) Change in the voice.
g) Regional (ipsilateral) lymphadenopathy.
h) Distant metastasis.
i) Symptoms of compression or infiltration, including dysphagia, dysphonia, hoarseness, dyspnoea, stridor, new snoring or cough.
j) Exposure to fallout from Chernobyl prior to 14 years of age or other ionising radiation.
k) Findings of vocal cord palsy on examination.

Clinicians should be *moderately* suspicious of thyroid cancer if the patient presents with any of the following:

a) Male sex.
b) History of head and neck irradiation, or total body irradiation for bone marrow transplantation.
c) A nodule of > 4.0 cm in diameter or partially cystic.
d) Recurrent cysts.
e) Nodules with positive uptake on PET scan.

Guidelines for Solitary Thyroid Nodule

1 Thyroid function testing is a key part of the assessment of a patient with a thyroid nodule.

2 A thyroid ultrasound is the most accurate method to evaluate thyroid nodules and is the procedure of choice in initial evaluation of the thyroid lump.

Nodules with benign features (U2) on US do not require an FNA UNLESS there is a significant risk of cancer. Clinical assessment is required to determine their optimum follow up. So, small stable lesions with no worrying features on US or on clinical history may be discharged.

Larger lesions, those with ongoing growth, and those with any of the characteristics associated with increased risk (a-k above) may undergo an initial FNA due to increased clinical suspicion and should be offered interval follow up even if Thy2– typically with a repeat US in 6 months. If the nodule remains stable with benign features on repeat USS the patient may be reassured this is benign. Surgery or radioactive iodine may be offered for nodules causing compressive or significant cosmetic symptoms, while smaller, euthyroid and asymptomatic nodules do not require long term follow up or treatment.

3 Ultrasound guided Fine Needle Aspiration Biopsy (FNAC) is indicated for nodules with any suspicious characteristics (U3 or above) – see page 4.

Nodules with indeterminate or suspicious (U3 or above) ultrasound characteristics but apparently benign Thy2 cytology need careful assessment with consideration of repeat US and FNA prior to discharge.

All FNA results of Thy 3 or above require discussion at the thyroid MDT.

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Special circumstances

Abnormal TFTs

Abnormal thyroid function test results do not alter the above pathway – i.e. thyrotoxicosis does not rule out the presence of a malignancy, but it is very rare and needs specific treatment. FNAC is recommended only if the clinical suspicion for thyroid malignancy is high in the presence of thyroid dysfunction.

If hypothyroidism is present with benign FNAC, then treat appropriately with thyroxine and reassess the nodule at three months. A raised TSH does not preclude malignancy and so an ultrasound with FNA if indicated is still recommended because the rate of malignancy in nodules is similar in thyroid glands involved in Hashimoto's disease as in normal glands.

If hyperthyroidism is present then long term treatment is generally with radioiodine rather than anti-thyroid drugs. Thyroid uptake scanning should be performed in patients presenting with a solitary nodule. If this confirms the presence of a hot nodule, the patient can be offered radio-iodine and no further imaging or evaluation is required unless the nodule fails to shrink after treatment. However, if the uptake scan shows no uptake, then the nodule still requires evaluation on its own merits, with ultrasound and FNA if indicated at presentation. If the FNA is benign, then the patients should be reassessed at three –six months in the usual way, and if the nodule is smaller, discharge to the GP for follow up.

Thyroxine suppression therapy to try and shrink nodules is no longer recommended due to the long term effects on bone (osteopenia /osteoporosis) and cardiovascular physiology (atrial fibrillation).

Pregnancy

Thyroid nodules found for the first time in pregnancy should be treated in exactly the same way as in the non-pregnant individual. If a Thy 3, 4 or 5 lesion is detected on FNAC in pregnancy, then surgery is recommended. There is no consensus as to whether this should be carried out during or after pregnancy, however it should always be done after 24 weeks of gestation to minimise the risk of miscarriage. Thyroid cancer discovered during pregnancy does not act more aggressively than in non-pregnant women, and delaying treatment does not adversely affect outcomes.

PET positive thyroid nodules

With increasing use of PET scanning, more asymptomatic thyroid nodules are being detected with positive FDG uptake. These patients do have an increased risk of thyroid malignancy - up to 30% if there is focal and intense SUV uptake and so PET positive thyroid nodules always require evaluation through the thyroid lump clinic and assessment by US and FNA.

Diagnostic category	Risk of malignancy (%)
Non-diagnostic for cytological diagnosis (Thy1/Thy1c)/Unsatisfactory	0−10
Non-neoplastic (Thy2/Thy2c)/Benign	0−3
Neoplasm possible – atypia/non-diagnostic (Thy 3a)/Atypia of undetermined significance or follicular lesion of undetermined significance	5−15
Neoplasm possible - suggesting follicular neoplasm (Thy 3f)/Follicular neoplasm or suspicious for a follicular neoplasm	15−30
Suspicious of malignancy (Thy4)	60−75
Malignant (Thy5)	97−100

All lesions classified as Thy 3, 4 or 5 should be discussed at the next thyroid cancer multi-disciplinary team meeting.

Clinical Audit Standards

Reduction in numbers of 'blind FNAC' carried out and a reduction in numbers of Thy1 aspirates, with a concurrent rise in early thyroid cancer detection

Summary of development and consultation process undertaken before registration and dissemination

These guidelines were written at the request of the East Anglia Thyroid Cancer Multi Disciplinary Team. This comprises of Endocrinologists, Oncologists, Endocrine Surgeons, Histopathologists, Nuclear Medicine, and Radiologists from the Norfolk and Norwich University Hospital, Ipswich Hospital, Queen Elizabeth Hospital, King's Lynn and James Paget Hospital in Great Yarmouth.

They were written after an update of the current relevant literature. Several drafts were distributed amongst the members of the East Anglia Thyroid Cancer Multi Disciplinary Team.

This version endorsed by: Consultant endocrinologists at NNUH, and members of the East Anglia Thyroid Cancer Multi Disciplinary Team.

This version has been endorsed by the Clinical Guidelines Assessment Panel.

Distribution list / dissemination method

Via the Trust intranet and regionally amongst the hospitals comprising the East Anglia Thyroid Cancer Multi Disciplinary Team.

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