Chapter 28
Thyroid cancer

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A. DIFFERENTIATED THYROID CANCER

1. Introduction

Thyroid nodules are common, the incidence of palpable nodules in women being approximately 5% and 1% in men. Use of ultrasound scanning (USS) substantially increases their detection in the general population to approximately 50–70%. Thyroid cancer remains rare, but evidence suggests an increasing incidence, although survival rates remain static.

Long term prognosis for differentiated thyroid cancer (DTC) is excellent, with survival rates for adults being 80–90% at 10 year follow up. Factors influencing prognosis include gender, age at presentation, histology and tumour stage. Accurate diagnosis, treatment and long-term follow up are essential to achieve and maintain excellent survival rates.

In recent years, there have been several sets of detailed guidelines published on the diagnosis and management of thyroid cancer. Two key ones are the Guidelines for the Management of Thyroid Cancer (2007) by the British Thyroid Association and Royal College of Physicians, and the Revised American Thyroid Association Guidelines (2009). These documents are extensive and cover every aspect of care in great detail. Patients may initially be seen by a surgeon, endocrinologist, clinical oncologist or nuclear medicine physician, who must be a core member of the thyroid cancer multidisciplinary team (MDT). The goals of treatment of DTC are set out in Table 1.

Table 1. Goals of treatment for differentiated thyroid cancer

- Remove the primary tumour and involved lymph nodes
- Minimise treatment related morbidity
- Allow accurate staging of the disease
- Facilitate post-operative treatment with Radioactive Iodine in appropriate patients
- Enable long-term surveillance for disease recurrence
- Minimise the risk of disease recurrence and distant metastases

2. Clinical presentation

In all cases, a detailed history, documenting in notes family history and previous exposure to ionising radiation is warranted.

2.1. Symptom needing immediate referral

Stridor associated with thyroid nodule/goitre.

2.2. Symptoms needing urgent GP referral (2 week wait rule)

These include hoarseness/voice changes associated with a nodule/goitre, thyroid nodule in a child, cervical lymphadenopathy associated with a thyroid nodule and/or rapidly enlarging painless thyroid mass over a period of weeks.

3. Assessment and staging

3.1. Recommended clinical investigations

These include:

- Clinical evaluation of thyroid, cervical and supraclavicular nodes
- Thyroid stimulating hormone (TSH)
- Fine needle aspiration cytology (FNAC) with or without USS guidance.
- Documented cytological score (Table 2)
- Core biopsy with or without USS guidance in suspected cases of lymphoma

Table 2. Thyroid FNAC diagnostic categories

Score	THY1	THY2	THY3 (Subdivided)	THY4	THY5
Diagnosis	A and C Non-diagnostic	A and C Non-neoplastic Consistent with colloid nodule/ thyroiditis	THY3F Follicular lesion Suspected follicular neoplasm THY3A Atypia present	Suspicious but not diagnostic of thyroid cancer (papillary, medullary, anaplastic, lymphoma)	Diagnostic of thyroid cancer (papillary, medullary, anaplastic, lymphoma)
Action	Repeat FNA Consider USS guidance Describe as cyst if no epithelial cells present	Repeat FNA if no surgery planned.	Discuss at multi-disciplinary team meeting (MDT) Diagnostic lobectomy usually recommended Consider total thyroidectomy in large lesions >4cm where incidence of malignancy is higher.	Discuss at MDT Diagnostic Lobectomy +/- on table frozen section to proceed to total thyroidectomy +/- central node clearance in high risk patients	Discuss at MDT Radiotherapy/ chemotherapy or surgery where indicated Appropriate further investigations for staging where indicated Total thyroidectomy +/- central node clearance in appropriate high risk patients

- Calcitonin only in suspected cases of MTC (routine use not recommended)
- Serum thyroglobulin (Tg) is not recommended
- Pre-operative vocal cord check

3.2. Radiological investigations

Pathological studies suggest that microscopic lymph node metastases are very common in papillary thyroid cancer, macroscopic disease less so (20–50%). Pre-operative USS is effective in identifying suspicious nodes in approximately 20–30% of patients with papillary thyroid cancer and may alter the surgical approach. FNA of suspicious nodes is recommended. Thyroglobulin estimation of lymph node cystic fluid may be of use in the absence of sufficient diagnostic material.

Recommendations

- USS guided FNAC for all patients with nodules over 10 mm should be done whenever possible (Grade B)
- If nodule below 10 mm USS guided FNA not recommended unless clinically suspicious nodes on USS are also present (Grade B)
- USS assessment is potentially of value in assessing co-existing dominant nodules (Grade B)
- Cytological analysis and categorization should be reported according to the current British Thyroid Association guidance (Grade B)
- USS assessment of cervical nodes should be done in FNA proven cancer (Grade B)
- MRI or CT (*without the use of iodinated contrast*) should be done in suspected cases of retrosternal extension, fixed tumours (local invasion +/- vocal cord paralysis) or when haemoptysis reported (Grade B)
- FDG-PET imaging is not recommended for routine evaluation

3.3. Staging

The TNM staging system (7th edition) for differentiated thyroid cancer is as follows:

T stage

T1	≤2 cm in greatest dimension limited to the thyroid.
	T1a ≤1 cm, limited to the thyroid.
	T1b >1 cm but ≤2 cm in greatest dimension, limited to the thyroid.
T2	>2 cm but ≤4 cm in greatest dimension, limited to the thyroid.
T3	>4 cm in greatest dimension limited to the thyroid or any tumor with minimal extrathyroid extension (e.g., extension to sternothyroid muscle or perithyroid soft tissues).
T4a	Tumor of any size extending beyond the thyroid capsule to invade subcutaneous soft tissues, larynx, trachea, esophagus, or recurrent laryngeal nerve.
T4b	Tumor invades prevertebral fascia or encases carotid artery or mediastinal vessels.
T4a	Intrathyroidal anaplastic carcinoma
T4b	Anaplastic carcinoma with gross extrathyroid extension.

N stage

N0	No regional lymph node metastasis.
N1	Regional lymph node metastasis.
	N1a Metastases to level VI (pretracheal, paratracheal, and prelaryngeal/Delphian lymph nodes).
	N1b Metastases to unilateral, bilateral, or contralateral cervical (levels I, II, III, IV, or V) or retropharyngeal or superior mediastinal lymph nodes (level VII).

M stage

M0	No distant metastasis..
M1	Distant metastasis

Group staging

	Under 45 years	**45 years and older**
Stage I	Any T, any N, M0	pT1, N0, M0
Stage II	Any T, any N, M1	pT2, N0, M0 pT3, N0, M0
Stage III		pT4, N0, M0 Any pT, N1, M0
Stage IV		Any pT, any N, M1

Undifferentiated or anaplastic carcinomas are all Stage IV

Recommendation

- All patients should be staged by clinical and pathological TNM staging (Grade B)

4. Management

Surgeons performing operations for confirmed or suspected thyroid cancer should be core members of the thyroid cancer MDT. Complex surgery and lymph node surgery should be undertaken by identified/nominated surgeons in the cancer centre with specific training in and experience of thyroid oncology. Table 3 lists patients deemed to be '*High Risk'* and these patients should be considered for level VI lymph node dissection (pre-tracheal and para-tracheal nodes from the hyoid bone superiorly to the level of the sternal notch inferiorly). Lobectomy should include the isthmus in all patients. Sub-total thyroidectomy is not an appropriate operation for thyroid cancer.

Frozen section histology may be of use in confirming suspected papillary thyroid cancer (THY4) but is not recommended for use in cases of suspected follicular thyroid cancer (THY3).

Table 3. High Risk DTC Patients

- Male
- Age >45 yrs
- Tumour >4cm
- Extra-capsular disease
- Extra-thyroidal disease

Recommendations

- The management of DTC and MTC should be the responsibility of a specialist multidisciplinary team, the membership of which should be appointed by the regional cancer network (Grade C)
- The multidisciplinary team should comprise of surgeon, endocrinologist, oncologist or nuclear physician with support from pathologist, medical physicist, radiologist and clinical nurse specialist all with expertise and interest in the management of thyroid cancers (Grade C)

4.1. Surgical treatment

4.1.1. Initial surgery for known papillary thyroid cancer

A strategy for the surgical treatment of papillary thyroid cancer is detailed in Table 4. All cases should be discussed pre-operatively at the thyroid cancer MDT

Table 4. Initial surgery for known papillary thyroid cancer

Recommendation	**Tumour <1cm**	**Tumours >1cm**	**T3 and T4 Tumours +N1 level VI Nodes**
	With no other clinical features such as extra-thyroidal spread, nodal involvement, etc	Papillary cancer diagnosed following thyroid lobectomy Multifocal disease Thyroid radiation in childhood Familial disease (1st degree)	Treat all above tumours as high risk
Thyroid lobectomy	Yes	No	No
Total thyroidectomy	Discuss at MDT	Completion total	Yes
Prophylactic level VI nodal dissection	No	In high risk patients	Yes
Therapeutic level VI nodal dissection (clinically involved)	Yes	Yes	Yes

4.1.2. Initial surgery for follicular thyroid cancer

The majority of patients undergoing surgery for follicular thyroid cancer will be undiagnosed at the time of the initial surgery (THY3). Frozen section histology is not recommended. An operative strategy for surgical treatment of follicular cancer is outlined in Table 5.

Low risk patients with a diagnosis of minimally invasive tumour, without vascular invasion, <2 cm following lobectomy may be managed by lobectomy and TSH suppression alone in most cases. No clear recommendations currently exist for low risk minimally invasive tumours of 2–4 cm and these cases should be discussed individually at MDT. In some cases lobectomy and TSH suppression alone may be sufficient.

Hurthle cell cancers (follicular oncocytic) tend to be more aggressive tumours and should be treated by total (completion) thyroidectomy (see Table 5).

Table 5. Initial surgery for follicular thyroid cancer

	Clinical Details	
Recommendation	**High Risk Patient** > 45 years Tumour > 4 cm Extracapsular invasion Extrathyroidal disease Hurthle cell tumours	**Low Risk Patient** Female < 45 years
Thyroid lobectomy	No	Yes
Total thyroidectomy	Yes	No
Level VI nodal dissection	Only where clinically involved nodes present	No

4.1.3. Management of lymph nodes in DTC

Therapeutic level VI nodal dissection is recommended when the presence of lymph node metastasis is confirmed by FNA / core or open biopsy/frozen section. Prophylactic level VI lymph node dissection is advised in high risk patients but is associated with a higher incidence of recurrent laryngeal nerve damage and long term permanent hypoparathyroidism, informed consent should reflect this. Prophylactic level VI nodal dissection is not recommended in low risk, small papillary and most follicular cancers.

Clinically involved lateral cervical lymph nodes should be managed by selective neck dissection (levels II-V). Isolated lymph node excision "berry picking" is not advocated. Involvement of level I or level VII nodes is rare in DTC and should only be dissected if involved. Prophylactic lateral neck compartment dissection for node negative (clinically/radiologically N0) patients is not recommended in DTC.

4.1.4 Completion thyroidectomy

Completion thyroidectomy is not needed in low risk, small (<1cm), unifocal, intrathyroidal, clinically node negative tumours.

4.1.5. Locally advanced disease

Where possible, locally advanced disease should be resected. In an attempt to perform curative resection unilateral RLN sacrifice may be necessary. Where both nerves are involved then residual tumour may be left to protect the nerve(s) and residual disease treated with external beam radiation and or radioiodine. Extensive resection of trachea, larynx and oesophagus should only be considered if potentially curative. Where disease is unresectable, radiotherapy and radioiodine should be considered.

Recommendations

- Surgeons performing surgery for thyroid cancer should have training and expertise in the management of thyroid cancer and be a member of the MDT (Grade C)
- The aims of the surgical procedure should be the removal of all tumour, elimination of clinical, radiological or biochemical evidence of recurrence and the minimisation of unwanted effects of the treatment (Grade B)
- Patients with a PTC more that 1 cm in diameter and high risk FTC should undergo total or near-total thyroidectomy (Grade B)
- Patients with low risk FTC or PTC less than 1 cm in diameter may be treated with thyroid lobectomy alone. (Grade B)
- Prophylactic central compartment neck dissection should be done for all tumours over 1cm in diameter in high risk patients or T2 to T4 tumours (Grade B)

4.2. Post-operative management

After total/near total thyroidectomy patients should be commenced on T3 (usually 20micrograms thrice daily). Calcium levels should be routinely checked within 24 hours and hypocalcaemia treated appropriately. Thyroglobulin (Tg) levels should be checked no earlier than 6 weeks after the operation.

All patients with DTC should be clinically staged using the TNM Classification (7th edition) and also scored using one of the clinico-pathological scoring systems to enable planned follow up, identification of high risk patients and those who would benefit from radio-iodine therapy.

In addition, all patients should have access to a thyroid clinical nurse specialist and be given written information.

4.3. Radioiodine ablation and external beam radiotherapy in DTC

The 2002 BTA UK Guidelines were in favour of virtually all patients with DTC <10 mm receiving I^{131} ablation. The 2007 BTA Guidelines along with their American counterpart the ATA 2009 Guidelines are less prescriptive. Table 6 outlines the current recommendations with regards to I^{131} ablation.

Table 6. Indications for I^{131} ablation post total/near thyroidectomy for DTC

Recommendation	Clinical Details
Definite I^{131} ablation	Tumour >4 cm, distant metastases, extra-thyroidal invasion, >10 involved nodes or >3 nodes with extra-capsular invasion
Probable I^{131} ablation **Consider on individual case merit (MDT)**	Tumour size <1cm where histology is associated with poorer prognosis Tumour size >1cm but <4 cm Multifocal tumours <1cm Lymph nodes not assessed at surgery Less than total thyroidectomy (consider further surgery to remove large remnant)
No I^{131} ablation	Multifocal tumours <1cm Unifocal cancer <1cm (favourable histology, N0 M0) Minimally invasive follicular cancer <2 cm without vascular invasion

Patients should be prepared by performing a pregnancy check where indicated, withdrawing T4 (2–4 weeks) or T3 (2 weeks), taking a thyroglobulin sample and ensuring that TSH is >30 mI U/L prior to I^{131} administration. Where T4 or T3 withdrawal is contraindicated or ineffective then rhTSH may be used.

Post-therapy diagnostic scanning assessing effectiveness of I^{131} therapy may be omitted in low risk patients if TSH stimulated Tg levels are checked along with USS of neck nodes. Otherwise diagnostic whole body scanning (WBS) scanning should always be performed 6 months after I^{131} ablation.

Adjuvant EBR should be considered in unresectable tumours in addition to I^{131} and where there is residual disease following surgical resection even if the residual tumour concentrates I^{131}.

4.4. Post-treatment follow up

Persistent voice dysfunction should be investigated and referral to a specialised practitioner for assessment and speech therapy sought. The British Association of Endocrine and Thyroid Surgeons (BAETS) currently recommend that all patients undergoing thyroid surgery should have a post-operative vocal cord check.

Patients with long-term hypocalcaemia (hypoparathyroidism) should have their calcium levels regularly monitored either in association with an endocrinologist or their general practitioner.

Long-term suppression of TSH to levels below 0.1mI U/L has been demonstrated to improve outcome in patients with high risk cancers. There is no evidence to support this in low risk patients. TSH suppression may lead to exacerbation of angina and increase the risk of atrial fibrillation and osteoporosis in post-menopausal women.

TSH suppression to below 0.1mI U/L is therefore recommended for all high risk patients whilst maintaining a TSH level at or just below the lower level of normal is appropriate for low risk patients.

4.4.1 Monitoring thyroglobulin (Tg) levels

Thyroglobulin monitoring is most effective following total/near total thyroidectomy and radio-iodine ablation and is an important modality in detecting residual or recurrent disease. Physicians should be aware that thyroglobulin estimations vary according to the assay method, the individual laboratory and the presence of anti-thyroglobulin antibodies (TgAb) and take these considerations into account when evaluating Tg levels in individual patients. The presence of TgAb may result in false negative serum Tg results and such data should be interpreted with caution. Increasing serum concentrations of anti-TgAb may be indicative of recurrent disease. During follow-up stimulated serum Tg levels after rhTSH administration are not comparable to those after thyroid hormone withdrawal, the latter generally tends to elicit a more robust Tg response than rhTSH.

Patient should have their Tg levels checked at 6–12 monthly intervals. Rising Tg levels are highly suspicious of recurrent disease. Tg evaluation is most effective following TSH stimulation, either by withdrawal of T4 or T3 or by direct rhTSH stimulation.

Following total/near total thyroidectomy and I^{131} ablation, *low risk patients* with undetectable Tg levels on TSH suppression should have a TSH stimulated Tg assessment along with USS of cervical nodes at 1 year following I^{131} ablation. If Tg levels remain undetectable following TSH stimulation then future recurrent disease is highly unlikely and patients may revert to yearly Tg estimation whilst remaining on TSH suppression.

Elevated Tg may be suggestive of recurrent/residual disease but is usually from a thyroid remnant. In low risk patients, an expectant policy can be maintained and repeated TSH stimulated assessment performed, Tg levels should fall. Rising or persistently elevated Tg needs further evaluation.

The use of rhTSH stimulated Tg estimation after I^{131} therapy is an established alternative to thyroid hormone withdrawal and should be considered in most cases. rhTSH is strongly indicated in the following cases: hypopituitarism, functional metastases (suppressing TSH), severe angina, advanced disease (frail patient) and history of psychiatric disturbance from hypothyroidism.

Second generation assays for serum Tg with functional sensitivity 0.05-0.1 mcg/l have recently been introduced. Using highly sensitive Tg assays, a serum Tg <0.1 while on suppressive thyroxine therapy has been shown to a negative predictive value greater than 98% for recurrent or persistent thyroid cancer and in such cases there may be no need for TSH stimulation.

4.4.2. Whole body I^{131} scanning (WBS) and USS

The majority of patients following I^{131} ablation will undergo WBS at 6-9 months after treatment. Low risk patients do not need further WBS and may be assessed as above. Further WBS is only deemed necessary in the presence of persistently raised or rising Tg levels whilst on TSH suppression or in high risk patients where TSH (or rhTSH) stimulated Tg levels rise, strongly suggesting recurrent disease.

Cervical USS to evaluate central and lateral nodes at regular intervals may be of value in high risk patients, and especially in patients where TgAb's interfere with the accuracy of Tg estimation.

Recommendations

- I^{131} ablation or therapy should be carried out only in centres with appropriate facilities (Grade C)
- Serum thyroglobulin and serum TgAb should be checked in all post-operative patients with DTC, but not sooner than 6 weeks after surgery (Grade C)
- Patients should be started on triidothyronine 20 µg tds after surgery and this should be stopped 2 weeks before I^{131} ablation or therapy (Grade C)
- The majority of patients with a tumour more than 1cm in diameter, who have undergone total or near-total thyroidectomy, should have I^{131} ablation or therapy (Grade B)
- A post-ablation scan should be performed 3 to 10 days after I^{131} ablation (Grade B)

4.5. Persistent, recurrent, loco-regional recurrence and distant metastases

Potentially resectable disease is best managed by surgery (including local cervical nodes and soft tissue disease in the neck), followed by I^{131}. Early detection and appropriate surgical intervention results in 30–50% of such patients becoming disease free. Residual disease not amenable to resection or resistant to I^{131} therapy is best treated with high dose palliative external beam radiotherapy.

Therapeutic central compartment +/- lateral and /or central nodal clearance should therefore be performed for all persistent/recurrent disease confined to the neck. Impalpable nodes >5–8 mm seen on USS or cross-sectional imaging following I^{131} therapy should be considered for removal. Removing nodes <5–8 mm has not be shown to be of benefit.

Where technically feasible, tumours invading the aero-digestive tract should be resected in combination with radiotherapy. Outcome is very dependent on completeness of resection and preservation of function. Great care should therefore be taken therefore in the selection and discussion of such patients at the MDT.

Distant metastases develop in 5–23% of patients with DTC. Sites not amenable to surgical resection should be treated with I^{131} therapy if iodine avid. Long-term survival may be expected in patients whose tumours take up I^{131}. Distant metastases are usually seen in the lungs and bones. There is no maximum limit to the cumulative dose of I^{131} that patients with persistent disease may receive and pulmonary fibrosis appears to be a rare side effect. Surgical resection of bony metastases should be considered (especially in patients <45 years of age), metastases not cured by I^{131} should be treated by radiotherapy. Other modalities such as intra-arterial embolisation, pamidronate infusion, radiofrequency ablation or vertebroplasty may be considered in cases of painful lesions.

Recommendations

- Potentially resectable recurrent or persistent disease should be managed with surgery whenever possible (Grade C)
- Distant metastases and sites not amenable to surgery should be treated with I^{131} therapy (Grade C)

4.6 Long term follow up

Lifelong follow up of DTC is recommended to monitor for late recurrence (often treatable and curable), effects of long-term TSH suppression (atrial fibrillation and osteoporosis) and late side effects of I^{131}. After 5 years of MDT follow up, low risk patients may be followed up in a nurse led clinic or via a primary care setting with defined parameters for further referral back to the MDT.

Clinical examination and history, thyroglobulin determination, TSH suppression and where necessary calcium monitoring should all be performed. USS as per established protocols may also be undertaken.

Recommendations

- Long term follow up for patients with DTC is recommended (Grade B)
- Follow up should be done with clinical examination, serum TG and TSH suppression (Grade B)

B. MEDULLARY THYROID CANCER (MTC)

1. Introduction

MTC is a rare cancer (approximately 5% of all thyroid cancer cases). All cases should be referred for surgical treatment to the designated cancer centre of the Thyroid Cancer Network. Twenty five percent of MTC cases are familial (MEN 2A, MEN 2B and familial non-MEN FMTC). Genetic screening (*RET* testing) of all patients is mandatory and the assessment and investigation treatment of family members at potential risk requires a multidisciplinary approach within the cancer centre.

2. Clinical presentation

Patients usually present clinically with a thyroid nodule or neck mass with or without cervical lymphadenopathy (in the same fashion as with DTC). History however, may reveal other symptoms such as flushing, loose stools or diarrhoea (which suggest MTC) and is vitally important in determining a potential familial element.

FNAC may be diagnostic (when combined with Calcitonin staining in suspicious cases) but often is reported as THY3.

3. Assessment and staging

When MTC is suspected (or proven) patients must undergo the following investigations prior to surgery:

i) Calcitonin and carcino-embryonic antigen (CEA) levels
ii) 24 hour urine estimation of catecholamines and metanephrines to identify or exclude phaeochromocytoma
iii) Serum calcium and parathormone to identify or exclude hyperparathyroidism
iv) CT, MRI or USS of the neck are desirable as they may help guide the extent of surgical resection at initial surgery.
v) *RET* proto-oncogene mutational analysis should be performed after surgery once diagnosis is established

Staging

TNM staging for MTC follows the same criteria than for DTC. The group staging is as follows:

Stage I	T1, N0, M0
Stage II	T2, T3, T4, N0, M0
Stage III	Any T, N1, M0
Stage IV	Any T, any N, M1

Recommendations

- Patients with suspected MTC should be investigated with calcitonin and CEA levels, 24 hour urine estimation, serum calcium and PTH (Grade B)
- Relevant imaging studies are advisable to guide the extend of surgery (Grade C)
- RET proto-oncogene analysis should be performed after surgery (Grade B)

4. Management

4.1. Surgery for MTC

All patients with MTC should undergo:-

i) Total thyroidectomy and central compartment node clearance (level VI). This should be performed even in the presence of disseminated metastases to control local disease
ii) Patients with clinically involved lateral compartment nodes should have a therapeutic lateral neck dissection to eradicate local disease.

iii) All T2–T4 tumours should also undergo bilateral selective neck dissection IIa-Vb (even in absence of clinically palpable disease).
iv) Intra-thoracic disease below the level of the brachiocephalic vein should be resected via sternotomy where feasible.
v) Prophylactic thyroidectomy should be offered to RET positive family members. Timing and extent of surgery is dependant on genotype (codon mutation), the calcitonin level and age at detection of RET positivity.

4.2. Persistent or recurrent MTC

Calcitonin levels are most informative 6 months after initial surgery. It is important to distinguish persistent loco-regional disease (following either inadequate initial surgery or local lymph node metastases) from distant disease.

Early local recurrence following adequate local surgery (total thyroidectomy and level VI nodes) is unusual. The likely source of raised calcitonin in this circumstance is the lateral compartment cervical nodes i.e. persistent disease. When indicated, re-operation including further central compartment surgery and lateral neck node dissection should be performed. The primary aim should always be to control local disease.

CT, MRI, USS, selective arteriography, I^{131} -MIBG, ^{18}FDG-PET, In^{111} -octreotide and direct laparoscopic visualisation of the liver may all be useful in identifying the source of a raised calcitonin but their use in patients with calcitonin levels < 400–500 pg/ml is unlikely to identify metastases. When indicated, isolated metastases should be considered for surgical resection.

Recommendations

- All patients with proven MTC should undergo total thyroidectomy and central compartment neck dissection even in the presence of distant metastases (Grade B)
- Patients with N+ neck disease or those with T2–T4 with N0 neck disease should undergo bilateral selective neck dissections (IIa-Vb) (Grade C)
- Prophylactic thyroidectomy should be offered to RET positive family members (Grade B)

4.3. Radiotherapy and chemotherapy

Radiotherapy is of use in controlling local symptoms in patients with inoperable disease and improving the relapse free rate following central or lateral compartment surgery where residual disease is present macroscopically or microscopically.

Chemotherapy has been generally ineffective, but the new tyrosine kinase inhibitors may offer an alternative treatment in alleviating symptoms with metastatic disease.

Somatostatin analogues may be effective in alleviating the unpleasant gastrointestinal symptoms that patients with advanced cases of MTC experience.

Recommendations

- Radiotherapy may be advisable in controlling local symptoms in patients with inoperable disease (Grade C)
- Chemotherapy with tyrosine kinase inhibitors may help in controlling local symptoms (Grade B)

5. Follow up

Lifelong follow up is recommended for all patients with MTC. Screening should include calcitonin and CEA. TSH suppression is not necessary. Rising calcitonin levels should trigger investigations to identify potentially treatable metastatic disease.

6. New treatments for advanced thyroid cancer

Several new agents including tyrosine kinase inhibitors appear to have efficacy in patients with advanced differentiated and medullary thyroid cancer. Patients who have progressive metastatic disease should be considered for enrolment in clinical trials.

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