

## ***Review Article***

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# **Management of papillary and follicular (differentiated) thyroid carcinoma-an update**

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### **Abstract:**

*Thyroid cancers are quite rare, accounting for only 1.5% of all cancers in adults and 3% of all cancers in children. Differentiated thyroid cancer comprises 95% of all thyroid cancers. Of all thyroid cancers 74-80% of cases are papillary cancers. Incidences of follicular carcinoma are higher in regions where incidence of endemic goiter is high. Surgery is the definitive management of thyroid cancer. There is agreement that patients with large, locally aggressive or metastatic differentiated thyroid cancer require total thyroidectomy but there is continuing disagreement on the most appropriate operation for 'low risk' differentiated thyroid cancer. Adjuvant treatments are thyroid hormone suppression and radioiodine therapy rather than chemotherapy and radiotherapy. Prognosis is generally excellent and is influenced by factors related to the patient, the disease and the therapy. This article reviews the basis of surgical treatment of differentiated thyroid cancer and assesses the evidences supporting the surgical options.*

**Key words:** *Papillary Carcinoma, Follicular Carcinoma, Hemithyroidectomy, Total Thyroidectomy*

### **Introduction:**

The incidence of differentiated thyroid cancer (DTC) has increased in many places around the world over the past three decades.<sup>1</sup> Most thyroid cancers grow slowly and are associated with very favourable prognosis. The mean survival rate after 10 years is higher

than 90% and is 100% in very young patients with minimal non-metastatic disease if treated appropriately.<sup>2</sup>

But long term relapse rate is high, in the order of 20-40%, depending upon the patient's age & tumour stage at the time of initial treatment. Although contemporary guidelines increasingly recommend total thyroidectomy for virtually all cancers, small follicular carcinoma of 1cm or less in size and papillary carcinomas that are well circumscribed, isolated and less than 1cm in a young patient (20-40years) without a history of radiation exposure may be treated with hemithyroidectomy and isthmusectomy.<sup>3</sup> Radioiodine therapy is an essential part of therapeutic regimens in almost all cases, and the use of recombinant human thyroid-stimulating hormone has established for ablation of remnant tissue treatment of iodine-

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positive cancer, and sensitive thyroglobulin measurement during follow-up.<sup>4</sup> For inoperable and radioiodine-negative thyroid carcinomas, novel treatment options such as tyrosine kinase inhibitor therapy have emerged.<sup>4</sup>

A literature search of all relevant articles was made. References from obtained articles were reviewed. Recent guidelines from National Cancer Institute, US National Institute of Health, British Thyroid Association, Royal College of Physicians and Surgeons, European Society for Medical Oncology (ESMO) Clinical Practice Guidelines were studied and co-coordinated which provide an excellent overview of surgical treatment of DTC.

Types and incidence of thyroid cancer:<sup>5</sup>

1. Papillary and/or mixed papillary / follicular-78%
2. Follicular and /or Hurthe cell-17%
3. Medullary -4%
4. Anaplastic-1%

Treatment options for patients with thyroid cancer-

Different types of treatment are available, some are currently used and some are being tested in clinical trials.

Four types of standard treatment are<sup>6</sup>

### 1. **Surgery**

Procedures available:

- a. Lobectomy /Hemithyroidectomy
- b. Near total thyroidectomy
- c. Total thyroidectomy
- d. Lymphadenectomy

### 2. **Radiation therapy-**

- A. Radioactive iodine
- B. External beam radiation: When a large, unresectable tumour is present and the uptake of

radioiodine is limited, when intractable bone pain exists, or if resection is not feasible, external beam radiation may be performed to control local tumour growth, including, but not limited to, the neck, lungs, mediastinum, bone, and CNS (stage T4).<sup>7</sup>

### 3. **Thyroid hormone therapy**

4. **Chemotherapy:** Chemotherapy with cisplatin or doxorubicin has limited efficacy, producing occasional objective responses (generally for short durations). Because of the high toxicity of chemotherapy with cisplatin or doxorubicin, chemotherapy may be considered in symptomatic patients with recurrent or advancing disease. However, chemotherapy could improve the quality of life in patients with bone metastases, but a standard protocol for chemotherapeutic management has not been developed.<sup>7</sup>

### **New type of treatment:**

**Targeted therapy-** Tyrosine kinase inhibitor therapy is a type of targeted therapy being studied in the treatment of cancer. Tyrosine kinase inhibitor block signals needed for tumour to grow.<sup>6</sup>

### **Surgical treatment of differentiated thyroid carcinomas:**

The mainstay of treatment for DTC is surgery.<sup>8,9,10</sup> Compliance with appropriate and clear definitions of surgical procedures is essential.<sup>11</sup> The initial treatment of DTC is total or near total thyroidectomy whenever the diagnosis is made before surgery & the node is >1cm, or regardless of the size & histology if there is metastatic, multifocal or familial DTC. Less extensive surgical procedures i.e hemithyroidectomy may be accepted in the

case of small, unifocal, intrathyroidal & of favourable histological type (classical papillary or follicular variant of papillary or minimally invasive follicular).<sup>12</sup> Proponents of conservative surgical therapy relate the low rate of clinical tumour recurrence (5-20%) despite the fact that small amounts of tumour cells can be found in up to 88% of the opposite lobe of thyroid tissues.<sup>3</sup>

Proponents of total thyroidectomy cite several large studies show that in experienced hands, the incidence of recurrent laryngeal nerve injury and permanent hypoparathyroidism are quite low (about 2%).<sup>3</sup> These studies show that patients with total thyroidectomy followed by radio-iodine therapy and thyroid suppression, have a significantly lower recurrence rate and lower mortality when tumour are greater than 1.5cm in diameter.<sup>3</sup> More-over, total or near total thyroidectomy facilitates total ablation with iodine-131.

The argument against total thyroidectomy is that increases the risk of surgical complications such as recurrent laryngeal nerve injury and hypoparathyroidism. The benefit of prophylactic central node dissection in the absence of evidence of nodal disease is controversial.<sup>13</sup> It is not indicated in follicular thyroid cancer. In patients with papillary carcinoma, lymph node in the central compartment (paratracheal and tracheoesophageal areas) and the ipsilateral supraclavicular area and lower third of the jugulocarotid chain should be dissected. A modified neck dissection is performed if there are palpable lymph node metastases in the jugulocarotid chain.<sup>1</sup>

#### **Follow-up:**

There is also controversy about the way the patient should be follow-up after thyroid surgery. Follow-up methods include clinical examination, TSH monitoring to ensure adequate suppression, diagnostic scan and

serum thyroglobulin measurement.<sup>14</sup> Approximately 4-6 weeks after thyroidectomy, patients must have radioiodine therapy to detect and destroy any metastasis and residual tissue in the thyroid.<sup>7</sup> Administer therapy until radioiodine uptake is completely absent. Radioiodine treatment may be used again 6-12 months after initial treatment of metastatic disease where disease recurs or has not fully responded. Administer the thyroid hormone replacement levothyroxine at 2.5-3.5 mcg/kg/d to the patients for life.<sup>7</sup>

#### **Discussion:**

There are a number of classifications in current use for the staging of thyroid cancer<sup>13</sup>. The tumour node metastasis (TNM) according to the American Joint Cancer classification (ATCC) is commonly used as it is easy to apply and a number of studies have shown that it correlates with outcome.<sup>15</sup> pT1, NO tumour corresponds to the 'low risk' differentiated thyroid carcinoma which is less than 1cm in diameter, unifocal and intralobar occurring in younger patients (20-40years) with favorable histology & can be treated with thyroid lobectomy. Treatment for all other stages of papillary & follicular (differentiated) thyroid cancer is total or near total thyroidectomy. National guidelines under the auspices of the British Thyroid Association recommend three-stage management approach for most patients, including total or near-total thyroidectomy, <sup>131</sup>I ablation and thyroid hormone suppression therapy.<sup>14</sup> The first management stage for those with tumour diameters >1cm includes total thyroidectomy with central node dissection and postoperative <sup>131</sup>I ablation. This treatment destroys residual thyroid tissue, including occult carcinoma, and facilitates subsequent detection o recurrent disease.<sup>14</sup> Radioiodine ablation may be given four weeks after surgery. After total thyroidectomy and <sup>131</sup>I ablation the second management stage

includes a diagnostic radioiodine scan and serum thyroglobulin estimation (after thyroxine withdrawal) at six months. If there is significant uptake in the neck, further  $^{131}\text{I}$  is administered and a post-treatment scan is performed. If there is no significant uptake in the neck, thyroxine is restarted and low-risk patients enter the third management stage. The third stage involves long-term follow-up to detect recurrent disease.<sup>14</sup>

In the earlier times risks of extensive surgery and problems of adequate hormone replacement deterred surgeons from performing total thyroidectomy.<sup>16</sup> As are in the twenty-first century we are confident that the technical aspects of safe total thyroidectomy are established and the thyroid hormone replacement and monitoring are readily available and accurate.<sup>16</sup> Therefore total thyroidectomy is increasingly advocated and performed even in patients with low risk thyroid carcinoma. Thyroglobulin is useful in follow-up of well differentiated carcinomas (if a total thyroidectomy has been performed). A high serum thyroglobulin level that has previously been low following total thyroidectomy especially if gradually increases with TSH stimulation is indicative of recurrence. A value of greater than 10ng/L is often associated with recurrence even if an iodine scan is negative. Treatment with  $^{131}\text{I}$  to ablate thyroid remnants & residual disease are independent prognostic variables formally influencing distinct tumour relapse & cancer death rates.<sup>1</sup> Optimal long term follow-up using serum thyroglobulin measurement & diagnostic whole body scans (DxWBS) and thyroid ablation requires high concentration of TSH.<sup>1</sup> The method of choice for preparation to perform radio-iodine ablation is based on the administration of recombinant human TSH (rhTSH) while the patient is on levo-thyroxine ( $\text{LT}_4$ ) therapy.<sup>17</sup> Alternately levo-thyroxine is withdrawn for 4 to 6 weeks produces

symptomatic hypothyroidism.<sup>1</sup> Patients with undetectable or low thyroglobulin concentration & persistent occult disease can be identified within first year after initial treatment by recombinant human (rh) TSH-stimulated serum thyroglobulin concentration greater than 2ng/L without performing DxWBS.<sup>1</sup>

### Conclusion:

The most common causes of death are local recurrence and pulmonary metastases. Locally recurrent tumour is resected surgically with subsequent  $^{131}\text{I}$  therapy. Recurrences outside the neck are most frequently in lung but are also seen in bone. Patients whose metastases take up  $^{131}\text{I}$  are treated with radioiodine.<sup>13</sup> Most patients with DTC can be cured. However, both the initial treatment and follow-up should be individualized according to prognostic indicators and any subsequent evidence of disease.

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