Therapeutic Controversy in Differentiated Thyroid Cancer and the Need for a Clinical Protocol

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Abstract

Thyroid cancer accounts for less than 1.5 % of all cases of malignancy. Over 85 % were found to be a differentiated thyroid cancer (papillary, follicular, Hurthle cell). While differentiated thyroid cancer remains one of the most curable of all cancers, patients with aggressive tumors are occasionally seen. The role of prognostic factors in guiding therapeutic decision is becoming more important, these are like patient- related factors and tumor-related factors. However, management of differentiated thyroid cancer continued to be controversial; especially in relation to the role of radioiodine therapy and the recommended doses. [1-4]

Keywords: differentiated Thyroid Cancer, Clinical Protocol, radioiodine therapy.

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Prognostic Factors

For patients with differentiated thyroid cancer, age at time of presentation, tumor size and presence of extrathyroid extension or initial distant metastatic lesions are the most important risk factors for both recurrence and cause-specific mortality. Lymph node metastasis seems to have little influence on the risk of death but does increase the risk of locoregional recurrence. Knowledge of these relevant prognostic variables has led to several prognostic scoring systems. [5]

Primary Surgical Treatment

Removal of most, if not all, of the thyroid gland facilitates total ablation with radioiodine. This may result in a lower recurrence rate in comparison to the more limited surgery since many papillary tumors are multifocal and bilateral. In low risk patients (those with papillary cancer < 1.5 cm if unifocal), a lobectomy may be appropriate.

In patients with papillary cancer, lymph nodes in the central compartment (paratracheal and tracheoesophagial) and ipsilateral supraclavicular area and lower third of juglocarotid chain should be dissected. Surgical re-exploration may be considered if neck ultrasonography or radioiodine scan shows significant remnant (e.g. uptake > 10 %) or cervical lymph node activity. [6, 7]

Radioiodine 131 Therapy

Radioiodine therapy plays a major diagnostic and therapeutic role in the management of patients with differentiated thyroid cancer. The reasons for radioiodine therapy post-thyroidectomy are:

- It destroys any remaining normal thyroid tissue, thereby increasing sensitivity of subsequent radioiodine scan and the specificity of serum thyroglobulin for the detection of persistent or recurrent disease.

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- Radioiodine therapy may destroy occult microscopic cancer.

There is controversy about the indications for radioiodine ablative therapy. Opinions vary from using it for all patients or to be more selective; meaning to use it in certain situations such as:

- Complete excision of tumor but high risk of relapse due to:
- Age <16 or > 45 years.
- Histologic subtypes (tall cell, columnar cell,or diffuse sclerosing papillary variants, poorly differentiated subtypes, Hurthle).
- Extent of tumor (large tumor mass, extension beyond the thyroid capsule or lymph node metastasis).
- Incomplete excision of tumor.
- Distant metastasis.

Also, there is different approaches for radioiodine ablation dose; low or high, fixed or calculated. The high fixed dose (75mci to 100mci) may be the most widely applied. Higher radioiodine therapeutic doses are given for lymph node metastasis, residual tumor or distant metastasis. [8, 12]

External Radiotherapy

It may be used in patients with poorly differentiated tumors that do not concentrate radioiodine, or in the post-operative management of patients with differentiated thyroid cancer who have gross evidence of local invasion and who are presumed to have residual disease. [13]

Chemotherapy

The use of chemotherapy is restricted to those tumors that are surgically unresctable, unresponsive to radioiodine and have been treated with external radiotherapy or not amenable to it. Doxorubicin may be the agent that appears to be effective. [14]

Thyroxine

The growth of thyroid tumor cells is TSH dependent and its inhibition with thyroxine may prevent recurrence and improve survival. The adequacy of therapy is monitored by measuring serum TSH which should be < 0.1Miu/L. But, in low- risk patients, TSH suppression should be less stringent and the goal for basal serum TSH should be in the 0.1 to 0.4 Miu/L range. [15]

Long- term Followup

No single diagnostic tool will detect all recurrences, that's why it is necessary to apply a series of overlapping strategies that include clinical examination, serum thyroglobulin, radioiodine wholebody scan, ultrasonography, and chest X-ray on periodic basis. In patients with elevated serum thyroglobulin and negative radioiodine scan, alternative imaging procedures are used: e.g. CT, MRI, Tc99M-MIBI scan and FDG-PET. The most common site of recurrence for papillary cancer is in cervical lymph nodes.

The primary therapy in this case is the surgical excision. Then radioiodine scan is performed to determine the need for any additional radioiodine treatment. [16-18]

Controversial issues in the management of thyroid cancer

- Extent of surgery, lymph node dissection, and re-exploration.
- Post-operative radioiodine neck scan and uptake or doing wholebody scan.
- The indications for radioiodine ablation therapy.
- Radioiodine ablative dose: calculated or fixed, low or high.
- Duration of admission and isolation, radiation protection measures and exposure rate threshold for discharge.
- The role of external beam radiotherapy.
- The role of chemotherapy.
- The appropriate dose of thyroxine.

- Management of elevated thyroglobulin and negative radioiodine scan.
- Management of Hurthle cell tumor.
- Management of brain metastasis.
- The maximum accumulated radioiodine dose.
- The role of recombinant h TSH.
- Long-term follow-up programme.

Because opinion varies on the management of differentiated thyroid cancer even in the different centers in the same country, there is a need for a clinical protocol that reflects the consensus opinion of endocrinology, surgery, nuclear medicine and radiation oncology, which may give guidelines for a multimodal therapy of differentiated thyroid cancer.

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تباين الآراء حول علاج سرطان الغدة الدرقية المتمايز والحاجة لوجود بروتوكول للعلاج

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الملخص

سرطان الغدة الدرقية المتمايز يشكل أكثر من 85% من حالات سرطان الغدة الدرقية. ومع أن الشفاء التام يتحقق في معظم الحالات، إلا أن بعض المرضى من الممكن أن يتعرضوا لخطر رجوع المرض وإنتشاره حتى يؤدي إلى الوفاة.

أما بالنسبة للعلاج فإن البحث عن أسلوب علاج مثالي لا يزال مثار جدل كبير. تعتبر الجراحة وهرمونات الدرقية واليود المشع الركائز الأساسية للعلاج، بينما من غير الشائع استخدام العلاج الشعاعي والكيماوي. إلا أن هناك قضايا تمتد إلى جوانب متعددة سواء فيما يتعلق بالعلاج الإبتدائي أو حول متابعة المرض. وما يثير الاهتمام، النقاش المستمر حول استخدام اليود المشع، فالآراء تتباين من حيث استخدامه في كل الحالات أو عند وجود المؤشرات المنذرة بالخطورة فقط. لذلك فإنّ من الضروري أن يوجد بروتوكول يشمل الوسائل المتعددة في علاج سرطان الغدة الدرقية المتمايز ويعبر عن هذا التباين في الآراء.

الكلمات الدالة: سرطان الغدة الدرقية المتمايز، هرمونات الغدة الدرقية، اليود المشع، بروتوكول.