

Update on Differentiated Thyroid Cancer Staging

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KEYWORDS

• Risk stratification • Differentiated thyroid cancer • Response to therapy

KEY POINTS

- An initial assessment of the risk of disease-specific mortality and the risk of persistent/recurrent disease is required to guide initial treatment and early follow-up and to set appropriate patient expectations with regard to likely outcomes after initial therapy.
- Although the American Joint Committee on Cancer/Union for International Cancer Control and MACIS (Metastases, Age, Completeness of Resection, Invasion, Size) staging systems provide valuable information regarding disease-specific survival, they do not adequately predict the risk of recurrent/persistent disease for individual patients; therefore, additional staging systems specifically developed to predict the risk of recurrent/persistent disease should be used to augment the information provided by staging systems designed to predict the risk of dying from thyroid cancer.
- Because all initial staging systems provide only a static initial risk assessment, ongoing management requires that these initial risk estimates continually be modified based on the biological behavior of the disease and the subsequent response to therapy.
- Although the dynamic risk assessment approach was originally proposed and validated in patients treated with total thyroidectomy and radioactive iodine (RAI) remnant ablation, by simply modifying the specific definitions of the response to therapy outcomes (excellent, indeterminate, and biochemically incomplete and structurally incomplete responses), we show how this same ongoing risk stratification approach can be applied to patients who have thyroid cancer treated with lobectomy or total thyroidectomy without RAI ablation.

INTRODUCTION

The last decade has seen a renewed interest in a risk-adapted approach to the management of differentiated thyroid cancer (DTC), in which specific treatment and follow-up recommendations are tailored to individualized estimates of risk.^{1–4} This customized management ensures that intensive treatment and follow-up studies are

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recommended for high-risk patients, who are most likely to benefit from an aggressive management approach, whereas low-risk patients are managed with a more conservative approach, designed to identify clinically important persistent/recurrent disease and to avoid exposure to the potential complications and side effects of excessive surgery, radioactive iodine (RAI) ablation, and subclinical hyperthyroidism. Therefore, the keystone for optimal management of DTC is accurate, real-time risk stratification.

From a practical clinical management standpoint, an initial assessment of the risk of dying from thyroid cancer and the risk of having persistent/recurrent disease is required to guide initial treatment, early follow-up and to set appropriate patient expectations with regard to likely outcomes after initial therapy.¹⁻⁴ Recent studies have emphasized the need for dynamic risk stratification during follow-up, in which the various clinical important risk estimates are modified over time as additional data are obtained during follow-up.⁵⁻⁹ These modified risk estimates reflect both the underlying biology of the disease and the response to initial (and subsequent) treatments and provide real-time risk estimates during follow-up, which may differ substantially from the initial risk estimates based only on clinicopathologic features available at the time of diagnosis and initial therapy.

In this review, the critical clinicopathologic risk factors commonly used in our modern staging systems are reevaluated and we then demonstrate how they are used to predict the risk of disease-specific mortality and recurrence is discussed. The concept and practical implementation of dynamic risk assessment are reviewed to explain our approach to long-term management. In previous work, this response to therapy evaluation system has been applied exclusively to patients who had total thyroidectomy and RAI ablation. In this review, this concept is expanded to include patients who did not require RAI ablation and those who were treated with less than total thyroidectomy.

Initial Risk Stratification

Initial risk stratification requires a detailed histologic description of the primary tumor and metastatic foci removed at the time of initial surgery and also a thorough understanding of other important preoperative and intraoperative findings (**Table 1**).^{10,11} These findings include preoperative evidence of gross extrathyroidal extension (hoarseness/stridor, fixation to surrounding structures), extensive locoregional metastases (clinical N1 disease), and distant metastases (symptomatic or incidentally found on preoperative imaging). Just as critical are the intraoperative findings of gross extrathyroidal extension (defined by involvement of the surrounding subcutaneous soft tissues, larynx, trachea, esophagus, or recurrent laryngeal nerve) and completeness of surgical resection, which can be major risk factors and are often not readily apparent in the written pathology report.¹²⁻¹⁸

Therefore, accurate initial risk stratification not only requires excellent, detailed histopathology reports but also relies on effective communication of critical findings among all members of the disease management team.¹⁰

Initial Estimates of Disease-Specific Mortality

A wide variety of staging systems have been used to predict the risk of death from DTC.¹⁹⁻³⁰ These staging systems take into account a relatively small set of clinicopathologic factors available at the time of initial therapy (**Table 2**). Nearly all of the staging systems use age at diagnosis, tumor size, the presence/absence of gross extrathyroidal extension and distant metastases as the primary variables. The extent of lymph node metastases is included in some of these systems and seems to convey an increased risk of mortality only in the setting of clinically significant metastatic lymphadenopathy (clinical N1 disease) in older patients.¹⁶

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