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# Prognostic factors in differentiated thyroid carcinoma

**KEYWORDS:** Thyroid Neoplasms; Prognosis

## ABSTRACT

*High cure rates are achieved after initial treatment of patients who develop differentiated thyroid cancer (DTC) and long-term outcome is usually favorable. However, some patients are at high risk of recurrence and even of death. These patients can be identified at the time of diagnosis by using well-established prognostic factors. The extents of primary operation on thyroid gland and regional lymph nodes, radioiodine ablation, as well as other treatment features still remain controversial. The most appropriate initial treatment can be applied and follow-up can be finely tailored. Prognostic factors for DTC are defined as specific features of patients (age, gender), tumors (histology, extent, aneuploidy), and treatment. During the past two decades the great efforts were made to establish the optimal prognostic scoring system that should include the most important prognostic factors for patients with differentiated thyroid carcinoma (DTC). The article reviews the chronology of prognostic scoring systems with their main characteristics in a goal to make easier the decision of adequate initial treatment modalities based on risk groups of patients with DTC.*

## INTRODUCTION

During the past two decades the great efforts were made to establish the optimal prognostic scoring system that should include the most important prognostic factors for patients with differentiated thyroid carcinoma (DTC). The extents of primary operation on thyroid gland and regional lymph nodes, radioiodine ablation, as well as other treatment features are remaining controversial.

High cure rates are achieved after initial treatment of patients who develop differentiated thyroid cancer (DTC) and long-term outcome is usually favorable. However, some patients are at high risk of recurrence and even of death. These patients can be identified at the time of diagnosis by using well-established prognostic factors. The most appropriate initial treatment can be applied and follow-up can be finely tailored. Prognostic factors for DTC are defined as specific features of patients (age, gender), tumors (histology, extent, aneuploidy), and treatment (1).

## EORTC SYSTEM

In 1979, Bayar and coworkers started a new era by publishing the EORTC prognostic system based on results of European multi-institutional multivariate analysis of prognostic factors in 507 patients with all types of thyroid cancer. They found age, histology type, distant metastases, extrathyroid extension and gender, to be independent prognostic factors for thyroid carcinomas (2).

## THE INSTITUTE GUSTAVE ROUSSY (IGR) SYSTEM

It was developed in 1985 in 546 patients with DTC without distant metastases at diagnosis. The system takes into account the two most relevant prognostic factors singled out in the cohort by multivariate analysis: age at diagnosis and the histological type. With these parameters, the authors defined two groups of patients:

- A group with a good prognosis, comprising patients (80%) below 45 years of age at diagnosis and who had a well-differentiated cancer (papillary or follicular) with a 25-year cancer-specific mortality rate of 2% and with mostly curable local recurrences.
- A group with a poor prognosis (25-year cancer-specific mortality rate of 30% and usually incurable local recurrences), comprising patients over 45 years of age or suffering from poorly-differentiated or widely invasive follicular thyroid cancer (2).

In the following years, authors from France (3,4), Scandinavia (5), and the Netherlands (6,7), have criticized EORTC system, on the basis of their results on 1813 patients with thyroid cancer.

## THE TNM STAGING SYSTEM (BY THE UICC)

It was introduced in 1987 and reviewed in 1992. Since 1988, it has been recognized as the reference international staging system. In the TNM system, DTC are staged separately from medullary and anaplastic carcinomas. It takes into account the age at diagnosis and is based on three variables: the extent of the primary tumor (T), the presence (N1) or absence (N0) of lymph node metastases and the presence (M1) or absence (M0) of distant metastases. This system defines 4 stages with increasing cancer specific mortality rate at 11.3 years: 1.7%, 15.8%, 30% and 60.9%, respectively (8).

## THE AGES AND MACIS SYSTEMS

Hay and coworkers from Mayo Clinic (1987) have suggested new prognostic scoring system, based on results of multivariate analysis on 1938 patients with differentiated thyroid carcinoma (DTC). They defined AGES system (age, tumor grade, local and distant extension, tumor size). They found that 86% of patients (group 1) have low (1%) cancer specific mortality rate, while others

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have higher mortality rate (24%, 49% and 93%, respectively) in 25-years follow-up (9).

In 1993, the same authors reviewed their scoring system, excluding tumor grade and including distant metastases, age, completeness of surgery, invasion of extra-thyroidal tissues and size (MACIS). The results of this cohort comprising 1779 patients with papillary thyroid cancer showed that 20-year survival rate was 99%, 89%, 56% and 24%, respectively for increasing scores (10). The value of this scoring system was confirmed in another study by the same authors based on 2512 patients with DTC followed from 1940 till 2000 (11).

### THE AMES AND DAMES PROGNOSTIC SYSTEM

The AMES system was created in 1988 by Cady and Rossi (Lahey Clinic). It is based on combination of age, distant metastases, and extent and tumor size. The AMES system defines a low-risk group (89%) of patients with DTC with mortality rate of 1.8%, and high-risk group (11%) with mortality rate of 46% in 20-year follow-up (12).

Paiseka and coworkers have suggested that adding a DNA ploidy to AMES system (DAMES) should increase the predictive value of AMES system (13).

### THE MEMORIAL SLOAN-KETTERING CANCER CENTER SYSTEM

In 1992, the authors have suggested that prognostic factors for DTC should be based on those related to patients and those related to tumor features. Besides low-risk (younger than 45 years with low risk tumor) and high-risk group (older than 45 with high risk tumor), they proposed intermediate risk group (younger than 45 with high-risk tumor and older than 45 with low-risk tumor). The long-term cancer specific survival was 99%, 87% and 57% in low-, intermediate-, and high-risk groups of patients (14).

### THE OHIO STATE UNIVERSITY SCORING SYSTEM

Back in 1994, Mazzaferri and his group have reported results of multivariate analysis of prognostic factors in DTC based on 1355 patients followed-up for 30 years. The scoring system does not include features related to patients - age at diagnosis and gender. Tumors are staged clinically into 4 categories according to tumors size, the presence or absence of neck lymph node metastases, multifocality, local tumor invasion, and distant metastases. Recurrence and mortality rates are respectively 8% and 0% in group 1 (13% of patients), 31% and 6% in group 2 (70% of patients), 36% and 14% in group 3 (15% of patients), and 62% and 65% in group 4 (2% of patients) (15).

Analyzing his own results and the results of similar comparative studies, Mazzaferri brings a critical review on therapy modalities and treatment results in patients with DTC. The age over 40 years at diagnosis, tumor stage (size, multifocality, local invasion, lymph node metastases), initial surgery at least "near" total thyroidectomy, radioiodine ablation are independent prognostic factors for DTC. Aggressive initial therapy gives a chance for complete cure in more than 90% of patients (16).

### CONCLUSION

The numerous, mostly retrospective studies, have shown that different prognostic factors have influence on recurrence and mortality rate in patients with DTC. They resulted in prognostic scoring systems that enables choosing adequate treatment modalities, especially extent of primary surgery, based on risk groups of patients.

The opposite opinions on the extent of primary operations have somehow become closer with fact that completeness of surgery is independent prognostic factor in MACIS system after 50 years follow-up. Some studies have shown that multifocality and presence of lymph node metastases are also independent prognostic factors for recurrence and survival rate in patients with PTC. All of these could provide arguments for more radical primary

surgery in differentiated thyroid carcinoma.

Nevertheless, experienced surgeon in this field perform these operations with minimal or no morbidity. That is why surgeon is a factor of prognosis both for long-term disease free survival and quality of life (17).

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