Thyroid

DOI: 10.1089/thy.2017.0102

The Updated AJCC/TNM Staging System for Differentiated and Anaplastic Thyroid Cancer (8th edition): What changed and why?

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Disclosure Statement: The authors have nothing to disclose

This work was funded in part by the NIH/NCI Cancer Center Support Grant P30 CA008748 (Craig Thompson, PI).

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In October 2016, the American Joint Committee on Cancer (AJCC; **www.cancerstaging.org**) published the 8th edition of the AJCC/TNM cancer staging system which will replace the 7th edition that has been in use by clinicians, cancer registries and researchers since 2009 (1). Unlike the American Thyroid Association (ATA) risk stratification system that is designed to predict disease recurrence, the AJCC/TNM system is optimized to predict survival in patients with cancer (2, 3). While clinicians are encouraged to use the scientific content of the 8th edition staging manual to enhance patient care, the actual implementation date for the 8th edition cancer staging system is planned to be 1 January 2018 in order to allow the cancer care community to make the infrastructure changes needed for data collection and implementation. All newly diagnosed cases through 31 December 2017 will continue to be staged by tumor registries according to the 7th edition staging system (https://cancerstaging.org/About/news/Pages/Implementation-of-AJCC-8th-Edition-Cancer-Staging-System.aspx). In this commentary, we will examine how the 8th edition differs from the 7th edition in the staging of differentiated and anaplastic thyroid cancers. Examination of the changes in the staging for medullary thyroid cancer will be presented in a follow up commentary in the near future.

Using an evidenced based medicine approach to literature review and grading, a multidisciplinary expert committee identified several specific areas in the 7th edition staging system that needed to be modified in order to optimize initial staging. While it is beyond the scope of this commentary to fully explore the reasons underpinning the changes in the 8th edition, the details and rationale for each of these changes with corresponding literature review is presented in the text of the 8th edition staging system

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for those interested in the details (1). As will be seen in the discussion below, the net effect of most of the changes in the 8th edition will be to downstage a significant number of patients into lower stages that more accurately reflect their low risk of dying from thyroid cancer. More individualized and accurate assessments of the risk of dying from thyroid cancer and the risk of disease recurrence should have a significant impact on both initial therapeutic decision making (e.g., extent of thyroid surgery, need for radioactive iodine ablation/therapy and/or need for TSH suppressive therapy) and on follow-up management strategies.

Description of the AJCC/TNM 8th edition staging system

The 8th edition T, N, and M definitions are presented in Figure 1 with the corresponding stages (I, II, III, and IV) presented in Figure 2 (1). In Table 1, we summarize the major changes to the AJCC/TNM staging of differentiated and anaplastic thyroid cancers in the 8th edition. While still retaining the basic anatomic pathology T-N-M staging approach, the 8th edition downstages a significant number of patients by (1) raising the age cut off from 45 years of age at diagnosis to 55 years of age, and (2) removing regional lymph node metastases and microscopic extrathyroidal extension from the definition of T3 disease. The 8th edition also re-emphasizes the critical importance of gross extrathyroidal extension as an unfavorable prognostic factor while minimizing the significance of minor extension through the thyroid capsule, which is identified only on histological examination. The 8th edition makes it clear that gross extrathyroidal extension is a clinical finding based on radiologic and/or clinical evidence of macroscopic tumor extending outside the thyroid gland. Consistent with previous editions, all data that is accumulated pre-operatively,

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intra-operatively and during the first 4 months of follow-up after thyroid surgery should be used to define the initial N and M status. The increase in the age cutoff from 45 years to 55 years of age at diagnosis downstaged a significant number of patients into stage I without significantly altering the mortality associated with the various stages (4). However, it is recognized that mortality increases progressively with advancing age beginning at about age 35 years. Thus any single cut point for age is likely to perform less well than models that consider age as a continuous variable (such as the MACIS system or nomograms (5-8).

Likewise, by removing lymph node metastases and minor extrathyroidal extension from the definition of T3 disease, a significant number of patients (45- 54 years old, N1, M0) will be downstaged to stage I and older patients will be downstaged to either stage I (≥ 55 years old, minor extrathyroidal extension, N0, M0) or stage II (≥ 55 years old, N1, M0). It does appear that the presence of clinically significant lymph node metastases is associated with poorer outcomes in adults of all ages, but the impact on survival in younger patients (< 55 years), even though statistically significant, is relatively minor (9) (hence classified as stage I) while the impact on survival in older patients is more clinically significant (hence classification as stage II disease). It is important to note that pathologic confirmation of lymph node status is not required and patients can be classified as having N0 disease as long as there is no evidence of lymph node metastasis on routine pre-operative and intra-operative evaluations (clinical examination, imaging, and intra-operative findings). As can be seen in Figure 1, the AJCC subclassifies N0 disease as either cytologically/histologically confirmed (N0a) or as the absence of radiologic or clinical evidence of disease (N0b). But in differentiated and anaplastic thyroid cancer, the subtype

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of N0 disease, location (N1a or N1b), or presence/absence of extranodal extension does not influence AJCC staging.

In addition to the critical factors necessary to appropriately stage patients (T, N, M), the 8th edition also provides a list of additional clinical factors that would be considered to aid in risk stratification for routine clinical care. These include presence/absence of microscopic extrathyroidal extension, the location of the involved lymph nodes (N1a vs. N1b), the number of involved lymph node, the number of lymph nodes sampled, the size of the largest involved lymph node, the size of the largest metastatic focus within a lymph node, the presence/absence of extranodal extension, the presence/absence of vascular invasion, the post-operative serum thyroglobulin, the completeness of surgical resection (R stage), and the specific histological subtypes. Currently, these additional clinical factors are useful in assessing the risk of recurrence and early response to therapy. It is likely that some of these additional clinical features may be incorporated into future editions of the AJCC/TNM staging systems to further refine and optimize initial risk stratification. Even though molecular characterization of tumors has the potential to refine risk estimates, none of the current molecular markers were considered to have sufficient independent prognostic significance to merit inclusion in the 8th edition staging definitions.

Comparison of the AJCC/TNM 7th and 8th edition staging systems

A comparison of the 7th edition and 8th edition staging system definitions and anticipated 10-year disease-specific survival rates are presented in the 8th edition text (1)

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and summarized in Table 2. The 10-year disease-specific survival rates presented in Table 2 represent our best estimates based on the published literature (see 8th edition text for detailed description and specific references (1)) but will require further studies involving long term follow-up in large multicenter data sets for validation and refinement.

For younger patients, the only differences in the definitions of stage I and stage II disease relate to the age cut off (45 years old in the 7th edition vs. 55 years old in the 8th edition). A recent international multi-institutional validation study of 9484 patients (median follow-up of 5 years) demonstrated that an increase in the age cut off from 45 years to 55 years of age at diagnosis downstaged 12% of patients and was associated with a 10-year disease-specific survival of 98% in the downstaged group (4). However, the very small number of patients that transitioned from 7th edition stage IV to 8th edition stage II (aged 45-54 with M1 disease, 29 out of 9484 patients, 0.3% of the entire cohort) demonstrated a 10-year disease-specific survival of 68% indicating that the increase in age cut off will move a few higher risk patients into the 8th edition younger stage II group (4). Nonetheless, since the majority of younger patients with M1 disease will do well, we anticipate that these small number of higher risk patients that are moved into the 8th edition stage II disease will have only a small impact on the long term disease-specific survival for this stage group.

In the older patients, there are significant differences in the staging definitions between the 7th and 8th editions. In the 8th edition, all patients with differentiated thyroid cancer ≤ 4 cm that is confined to the thyroid will be stage I while the 7th edition had previously classified smaller tumors (≤ 2 cm) as stage I and larger tumors (2-4 cm) as stage II. Since the disease-specific survival did not differ by tumor size for these intrathyroidal

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lesions, it was appropriate to combine these tumors into a single stage group (8th edition stage I).

In the 8th edition, older patients (> 55 years old) with metastatic spread to either central or lateral neck lymph nodes or gross extrathyroidal extension involving only the overlying strap muscles will be classified as stage II disease. Since lymph node metastases and gross extrathyroidal extension in these older patients are important prognostic factors, we expect stage II disease to have a 10-year disease-specific survival than is worse than stage I disease (See Table 2).

Stage III in the 7th edition included patients at relatively low risk of dying from thyroid cancer (primarily patients with central neck lymph node metastases and or microscopic extrathyroidal extension) while stage III in the 8th edition is composed of high risk patients demonstrating gross extrathyroidal extension into major structures in the neck without distant metastases at diagnosis. The 8th edition stage III patients should have outcomes slightly worse than the 7th edition stage IVa disease (T4a disease or N1b disease without distant metastasis) in which 10-year disease-specific survival approximated 75% (10). Therefore, the 8th edition stage III is expected to have a significantly poorer disease-specific survival than the 7th edition stage III category (See Table 2).

Similarly, stage IV in the 7th edition included all patients with gross extrathyroidal extension or distant metastases at diagnosis but also included all patients with lateral neck lymph node involvement, which, as mentioned above, is not associated with a high risk of early death from thyroid cancer. Conversely, stage IV in the 8th edition, excludes patients with just lateral neck lymph node metastases and includes only the patients at highest risk of dying from thyroid cancer (≥ 55 year old with extensive gross extrathyroidal extension

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defined as T4b disease or distant metastases at diagnosis). As a result, the 8th edition classifies fewer patients as having stage IV disease, but conveys a much poorer prognosis for this category than would have been predicted using the 7th edition definition that included patients without distant metastases with T4b or N1b disease.

With regard to anaplastic cancer, the major change involves the definition of the T category. In the past, all anaplastic thyroid cancer was classified as T4 disease with intrathyroidal disease classified as T4a and tumors with gross extrathyroidal extension were classified as T4b disease. For uniformity, the anaplastic thyroid cancer T category in the 8th edition will follow the same definitions as those used for differentiated thyroid cancers (See Figure 1). However, the stage groups remain effectively the same with intrathyroidal disease classified as stage IVA, while the presence of lymph node metastases or gross extrathyroidal extension mandates stage IVB and distant metastases are classified as IVC disease.

Practical application of the AJCC/TNM 8th edition staging system in clinical practice

From a practical implementation standpoint, we find it easier to rearrange the 8th edition staging table so that the proper stage can be easily identified based on the most important clinical factors (age, distant metastases and the presence or absence of gross extrathyroidal extension) as presented in Table 3.

- In patients less than 55 years old, all patients are stage I (regardless of tumor size, lymph node status, histological subtype or the presence/absence of extrathyroidal extension) unless they have distant metastases in which case they are stage II.

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- In patients 55 years of age or older, the presence of distant metastases mandates classification as stage IVB while older patients without distant metastases are further characterized based on the presence/absence of gross extrathyroidal extension, tumor size and lymph node status.
- Older patients with tumors ≤ 4 cm (T1-2) are stage I if confined to the thyroid (N0/Nx) or stage II if lymph node metastases are present (N1a or N1b).
- Older patients with tumors > 4 cm confined to the thyroid (T3a) are classified as stage II regardless of the lymph node status.
- Older patients demonstrating gross extrathyroidal extension are classified as stage II if only the strap muscles are grossly invaded (T3b), stage III if there is gross invasion of the subcutaneous tissue, larynx, trachea, esophagus or recurrent laryngeal nerve (T4a) and stage IVA if there is gross invasion of the prevertebral fascia or tumor encasing major vessels (T4b).

Conclusions

In summary, the net effect of the changes in the 8th edition staging system for differentiated thyroid cancer will be to appropriately classify the vast majority of thyroid cancer patients as being at low risk for dying from thyroid cancer (stage I or stage II disease). However, it is important to remember that the risk of death from thyroid cancer does not parallel the risk of recurrence in many patients. This is particularly true in the younger (< 55 years old) patients with stage I disease as this cohort will include the full spectrum of recurrence risk ranging from patient at very low risk of recurrence to patients at high risk of recurrence. Therefore, clinical management should be guided both by an

assessment of the risk of dying from thyroid cancer and the risk of recurrence. We endorse the management approach described in the recent ATA guidelines in which initial risk estimates (for both risk of recurrence and risk of dying from thyroid cancer) are formulated based on all the information available at diagnosis and are then modified over time as new data becomes available (2). This dynamic risk assessment approach will further refine the initial risk estimates and identify patients that are doing worse (or better) than would have been predicted by their initial staging. While additional studies are needed to provide further validation of this updated staging system, we see the 8th edition as a significant step forward in initial risk stratification for patients with differentiated thyroid cancer.

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References

1. Tuttle M, Morris LF, Haugen B, Shah J, Sosa JA, Rohren E, Subramaniam RM, Hunt JL, Perrier ND 2017 Thyroid-Differentiated and Anaplastic Carcinoma (Chapter 73). In: Amin MB, Edge SB, Greene F, Byrd D, Brookland RK, Washington MK, Gershenwald JE, Compton CC, Hess KR, Sullivan DC, Jessup JM, Brierley J, Gaspar LE, Schilsky RL, Balch CM, Winchester DP, Asare EA, Madera M, Gress DM, Meyer LR, (eds) AJCC Cancer Staging Manual. 8th ed. Springer International Publishing, New York City.

2. Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, Pacini F, Randolph GW, Sawka AM, Schlumberger M, Schuff KG, Sherman SI, Sosa JA, Steward DL, Tuttle RM, Wartofsky L 2016 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. Thyroid **26**:1-133.

3. Momesso DP, Tuttle RM 2014 Update on differentiated thyroid cancer staging. Endocrinol Metab Clin North Am **43**:401-421.

4. Nixon IJ, Wang LY, Migliacci JC, Eskander A, Campbell MJ, Aniss A, Morris L, Vaisman F, Corbo R, Momesso D, Vaisman M, Carvalho A, Learoyd D, Leslie WD, Nason RW, Kuk D, Wreesmann V, Morris L, Palmer FL, Ganly I, Patel SG, Singh B, Tuttle RM, Shaha AR, Gonen M, Pathak KA, Shen WT, Sywak M, Kowalski L, Freeman J, Perrier N, Shah JP 2016 An International Multi-Institutional Validation of Age 55 Years as a Cutoff for Risk Stratification in the AJCC/UICC Staging System for

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Well-Differentiated Thyroid Cancer. Thyroid **26**:373-380. doi: 310.1089/thy.2015.0315. Epub 2016 Feb 1025.

5. Ganly I, Nixon IJ, Wang LY, Palmer FL, Migliacci JC, Aniss A, Sywak M, Eskander AE, Freeman JL, Campbell MJ, Shen WT, Vaisman F, Momesso D, Corbo R, Vaisman M, Shaha A, Tuttle RM, Shah JP, Patel SG 2015 Survival from Differentiated Thyroid Cancer: What Has Age Got to Do with It? Thyroid **25**:1106-1114.

6. Hay ID, Bergstralh EJ, Goellner JR, Ebersold JR, Grant CS 1993 Predicting outcome in papillary thyroid carcinoma: development of a reliable prognostic scoring system in a cohort of 1779 patients surgically treated at one institution during 1940 through 1989. Surgery **114**:1050-1057; discussion 1057-1058.

7. Pathak KA, Mazurat A, Lambert P, Klonisch T, Nason RW 2013 Prognostic nomograms to predict oncological outcome of thyroid cancers. J Clin Endocrinol Metab **98**:4768-4775.

8. Adam MA, Thomas S, Hyslop T, Scheri RP, Roman SA, Sosa JA 2016 Exploring the Relationship Between Patient Age and Cancer-Specific Survival in Papillary Thyroid Cancer: Rethinking Current Staging Systems. J Clin Oncol **34**:4415-4420. Epub 2016 Oct 4428.

9. Adam MA, Pura J, Goffredo P, Dinan MA, Reed SD, Scheri RP, Hyslop T, Roman SA, Sosa JA 2015 Presence and Number of Lymph Node Metastases Are Associated With Compromised Survival for Patients Younger Than Age 45 Years With Papillary Thyroid Cancer. J Clin Oncol **33**:2370-2375.

10. Verburg FA, Mader U, Tanase K, Thies ED, Diessl S, Buck AK, Luster M, Reiners C 2013 Life expectancy is reduced in differentiated thyroid cancer patients >/= 45 years old with extensive local tumor invasion, lateral lymph node, or distant

metastases at diagnosis and normal in all other DTC patients. J Clin Endocrinol Metab **98**:172-180.

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Table 1: Major changes to the AJCC/TNM staging of differentiated and anaplastic thyroid cancers in the 8th edition.

DTC	**1.**	The age cutoff used for staging was increased from 45 to 55 years of age at diagnosis.
	2.	Minor extrathyroidal extension detected only on histological examination was removed from the definition of T3 disease and therefore has no impact on either T category or overall stage.
	3.	N1 disease no longer upstages a patient to stage III. If < 55 years of age at diagnosis, N1 disease is stage I. If ≥ 55 years of age, N1 disease is stage II.
	4.	T3a is a new category for tumors > 4 cm confined to the thyroid gland
	5.	T3b is a new category for tumors of any size demonstrating gross extrathyroidal extension into strap muscles (sternohyoid, sternothyroid, thyrohyoid, or omohyoid muscles)
	6.	Level VII lymph nodes, previously classified as lateral neck lymph nodes (N1b) were re-classified as central neck lymph nodes (N1a) to be more anatomically consistent and because level VII presented significant coding difficulties for tumor registrars, clinicians, and researchers.
	7.	In differentiated thyroid cancer, the presence of distant metastases in older patients is classified as IVB disease rather than IVC disease. Distant metastasis in anaplastic thyroid cancer continues to be classified as IVC disease.
Anaplastic	**1.**	Unlike previous editions where all anaplastic thyroid cancers were classified as T4 disease, anaplastic cancers will now use the same T definitions as differentiated thyroid cancer.
	2.	Intrathyroidal disease is stage IVA, gross extrathyroidal extension or cervical lymph node metastases is stage IVB, and distant metastases are stage IVC

Table 2: Comparison of the AJCC 7th and 8th edition staging system.

	Stage	7th Edition Description	7th Edition 10 yr DSS	8th Edition Description	8th Edition Expected 10 yr DSS
Younger patients	**I**	< 45 years old All patients without distant metastases regardless of tumor size, lymph node status or extrathyroidal extension	97-100%	< 55 years old All patients without distant metastases regardless of tumor size, lymph node status or extrathyroidal extension	98-100%
	II	< 45 years old Distant metastases	95-99%	< 55 years old Distant metastases	85-95%
Older patients	**I**	≥ 45 years old ≤ 2 cm tumor Confined to the thyroid	97-100%	≥ 55 years old ≤ 4 cm tumor Confined to the thyroid	98-100%
	II	≥ 45 years old 2-4 cm tumor Confined to the thyroid	97-100%	≥ 55 years old Tumors > 4cm, Or tumors of any size with central or lateral neck lymph nodes, Or gross extrathyroidal extension into strap muscles	85-95%
	III	≥ 45 years old >4 cm tumor, Or minimal extrathyroidal extension, Or central neck lymph node metastasis	88-95%	≥ 55 years old Tumors of any size with gross extrathyroidal extension into subcutaneous tissue, larynx, trachea, esophagus, recurrent laryngeal nerve	60-70%
	IV	≥ 45 years old Gross extrathyroidal extension, Or lateral neck lymph node metastasis, Or distant metastasis	50-75%	≥ 55 years old Tumors of any size or lymph node status with gross extrathyroidal extension into prevertebral fascia, encasing major vessels Or distant metastasis	< 50%

Table 3: A clinically based approach to staging in differentiated thyroid cancer using the 8th edition AJCC/TNM update.

	Distant Metastasis	Gross ETE present?	Structures involved with gross ETE	T category	N Category	Stage
< 55 yrs	**No**	**Yes or No**	**Any or None**	**Any**	**Any**	**I**
	Yes	**Yes or No**	**Any or None**	**Any**	**Any**	**II**
≥ 55 yrs	**No**	**No**	**None**	**≤4 cm (T1-2)**	**N0/Nx**	**I**
					N1a/N1b	**II**
				> 4 cm (T3a)	**N0/Nx/N1a/N1b**	**II**
		Yes	**Only strap muscle (T3b)**	**Any**	**Any**	**II**
			Subcutaneous, larynx, trachea, esophagus, recurrent laryngeal nerve (T4a)	**Any**	**Any**	**III**
			Prevertebral fascia, encasing major vessels (T4b)	**Any**	**Any**	**IVA**
	Yes	**Yes or No**	**Any or None**	**Any**	**Any**	**IVB**

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Legends for Figures and Tables

Definition of Primary Tumor (T)

For Papillary, Follicular, Poorly differentiated, Hurthle cell and Anaplastic Thyroid Carcinoma

T Category	*T Criteria*
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor ≤ 2 cm in greatest dimension limited to the thyroid
T1a	Tumor ≤ 1 cm in greatest dimension limited to the thyroid
T1b	Tumor > 1 cm but ≤ 2 cm in greatest dimension, limited to the thyroid
T2	Tumor > 2 cm but ≤ 4 cm in greatest dimension limited to the thyroid
T3*	Tumor > 4cm limited to the thyroid, or gross extrathyroidal extension invading only strap muscles
T3a*	Tumor > 4 cm limited to the thyroid
T3b*	Gross extrathyroidal extension invading only strap muscles (sternohyoid, sternothyroid, thyrohyoid, or omohyoid muscles) from a tumor of any size
T4	Includes gross extrathyroidal extension into major neck structures
T4a	Gross extrathyroidal extension invading subcutaneous soft tissues, larynx, trachea, esophagus, or recurrent laryngeal nerve from a tumor of any size
T4b	Gross extrathyroidal extension invading prevertebral fascia or encasing carotid artery or mediastinal vessels from a tumor of any size
Note: All categories may be subdivided: (s) solitary tumor and (m) multifocal tumor (the largest tumor determines the classification).	

Definition of Regional Lymph Node (N)

N Category	*N Criteria*
NX	Regional lymph nodes cannot be assessed
N0	No evidence of regional lymph nodes metastasis
N0a*	One or more cytological or histologically confirmed benign lymph node
N0b*	No radiologic or clinical evidence of locoregional lymph node metastasis
N1*	Metastasis to regional nodes
N1a*	Metastasis to level VI or VII (pretracheal, paratracheal, or prelaryngeal/Delphian or upper mediastinal) lymph nodes. This can be unilateral or bilateral disease.
N1b*	Metastasis to unilateral, bilateral, or contralateral lateral neck lymph nodes (Levels I, II, III, IV, or V) or retropharyngeal lymph nodes

Definition of Distant Metastasis (M)

M Category	*M Criteria*
M0	No distant metastasis
M1	Distant metastasis

Figure 1: 8th edition definitions for primary tumor (T), lymph node status (N) and distant metastasis (M). Changes from the 7th edition are marked with an asterix (See text for descriptions).

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Differentiated thyroid cancer

When age at diagnosis is…	***And T is…***	***And N is…***	***And M is…***	***Then the stage group is…***
< 55 yrs	Any T	Any N	M0	I
	Any T	Any N	M1	II
≥ 55 yrs	T1	N0/NX	M0	I
	T1	N1	M0	II
	T2	N0/NX	M0	I
	T2	N1	M0	II
	T3a/T3b	Any N	M0	II
	T4a	Any N	M0	III
	T4b	Any N	M0	IVA
	Any T	Any N	M1	IVB

Anaplastic thyroid cancer

T is…	***And N is…***	***And M is…***	***Then the stage group is…***
T1-T3a	N0/NX	M0	IVA
T1-T3a	N1	M0	IVB
T3b	Any N	M0	IVB
T4	Any N	M0	IVB
Any T	Any N	M1	IVC

Figure 2: 8th Edition AJCC prognostic stage groups for differentiated thyroid cancer (top panel) and anaplastic thyroid cancer (bottom panel)