

# Comparison of long-term prognosis for differentiated thyroid cancer according to the 7th and 8th editions of the AJCC/UICC TNM staging system

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## Abstract

**Background:** The 8th edition of the American Joint Committee on Cancer/Union for International Cancer Control (AJCC/UICC) tumor-node-metastasis (TNM) staging system was released with major revisions. The purpose of this retrospective study was to investigate differences between the 7th and 8th editions of the AJCC/UICC TNM staging system and to compare the predictability of prognosis between the two staging systems with patients who underwent thyroidectomy for differentiated thyroid cancer (DTC) at a single institution.

**Methods:** A total of 3238 patients underwent thyroid operation from January 2002 to December 2006 at Yonsei University Hospital (Seoul, Korea), of which 2294 with complete clinical data and sustained follow up were enrolled. Clinicopathologic features and TNM staging by applying the 7th and 8th editions of the AJCC/UICC were analyzed retrospectively by the complete review of medical charts and pathology reports of patients. Mean follow-up duration was  $132.9 \pm 27.9$  months.

**Results:** A significant number of T3 patients were downstaged to T1 (838, 36.5%) and T2 (122, 5.3%). After applying the 8th edition of the AJCC/UICC TNM staging system, the number of stage I patients increased significantly from 1434 (62.5%) to 2058 (89.7%), whereas numbers of stage III and IV patients decreased significantly from 644 (28.1%) to 33 (1.4%) and from 199 (8.7%) to 17 (0.7%), respectively. According to Kaplan–Meier survival analyses and values of the Harrell’s c-index and integrated area under the curve (iAUC), the 8th edition has significantly better predictive performance for disease-free survival (DFS) and disease-specific survival (DSS) than the 7th edition.

**Conclusions:** A significant population was downstaged after applying the 8th edition of the AJCC/UICC TNM staging system, and the 8th edition provided significantly better accuracy in predicting DFS and DSS in patients with DTC.

**Keywords:** differentiated thyroid cancer, disease-free survival, disease-specific survival, the 7th and 8th edition of the AJCC/UICC TNM staging system

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## Introduction

Differentiated thyroid cancer (DTC) has been increasing significantly over the last several decades. DTC is the most common endocrine malignancy, and its incidence accounts for 1–1.5% of all cancers.<sup>1–3</sup> According to cancer

statistics in Korea, thyroid cancers have been the most frequently diagnosed recently.<sup>4</sup> Papillary thyroid cancer (PTC) is the most common malignancy of the thyroid gland, accounting for 80% of all thyroid malignancies, and the second most common malignancy is follicular

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thyroid cancer.<sup>5</sup> DTC has excellent prognosis due to indolent features, and overall survival rate is over 90%.<sup>6</sup> Despite its excellent prognosis, prediction of prognosis is significantly important for the management of patients with DTC.

The American Joint Committee on Cancer (AJCC)/Union for International Cancer Control (UICC) tumor-node-metastasis (TNM) staging system has been used widely for predicting the prognosis of DTC in clinical practice. However, the staging system of DTC has remained unchanged since the 6th edition in 2002. The 8th edition of the AJCC/UICC TNM staging system was released in late 2016 and has been applied to all patients with DTC since 1 January 2018. The most significant differences between the 7th and 8th editions are the change in cutoff age, categorization of T3 disease, extent of N1a, and changes in TNM staging.

The cutoff age increased from 45 to 55 years in the 8th edition of the AJCC/UICC TNM staging system. Several studies suggested that extending the cutoff age to 55 years would lead to downstaging and improve the predictability of the TNM staging system.<sup>7–9</sup> The definition of T3 disease changed as well. According to the 7th edition of the AJCC/UICC TNM staging system, T3 was defined as tumors of >4 cm in the greatest dimension limited to the thyroid, or any tumor with minimal extrathyroidal extension (ETE). However, several studies have reported no significantly different prognosis between patients with minimal ETE and those with no ETE.<sup>10–13</sup> T3 was divided into T3a and T3b in the 8th edition of the AJCC/UICC TNM staging system. T3a was defined as tumors of >4 cm in the greatest dimension and limited to the thyroid, and T3b was defined as gross ETE invading only the strap muscles. According to the 8th edition of the AJCC/UICC TNM staging system, the definition of N1a was changed from only metastasis of level VI to metastasis of level VI including level VII.

The purpose of this retrospective study was to investigate differences between the 7th and 8th editions of the AJCC/UICC TNM staging system and to compare the predictability of prognosis between the two staging systems with patients who underwent thyroidectomy with DTC at a single institution.

## Materials and methods

### Patients

Clinicopathologic characteristics of 3238 patients who underwent thyroid operations from January 2002 to December 2006 were reviewed retrospectively at Yonsei university Hospital (Seoul, Korea). Of the total, 944 patients were excluded because of inadequate follow-up data and follow-up loss. For the remaining 2294 patients, clinicopathologic features and TNM staging applying the 7th and 8th editions of the AJCC/UICC were analyzed retrospectively by the complete review of medical charts and pathology reports of patients. Regarding surgical intervention, 658 (28.7%) patients underwent less than total thyroidectomy with prophylactic or therapeutic central compartment neck dissection (CCND), and 1636 (71.3%) underwent total thyroidectomy (TT) with prophylactic or therapeutic CCND. Among patients who underwent TT, 322 (14.0%) underwent modified radical node dissection (mRND) due to clinically suspicious or pathologically confirmed N1b nodes. The mean follow-up duration was 132.9 months (range, 105–160.8 months). This study was approved by the local institutional review board (IRB No.: 4-2017-0693), which waived the requirement for informed consent due to the retrospective nature of this study.

### Postoperative management and follow up

The management protocol was followed using the American Thyroid Association (ATA) management guidelines. Of the total patients, 1609 (70.1%) received radioactive iodine (RAI) ablation at 4–8 weeks after operation. Thyroglobulin (Tg) and anti-thyroglobulin antibody (TgAb) concentrations were measured after thyroid stimulating hormone (TSH) stimulation by thyroid hormone T4 withdrawal or recombinant human TSH injection before RAI ablation. Whole body scans (WBSs) were performed 5–7 days after RAI ablation. Patients were followed up by physical examination, neck ultrasonography, and the measurement of serum Tg and TgAb concentrations at 3 and 6 months, and annually thereafter. Patients who had evidence of recurrence or distant metastasis on routine follow-up evaluations were assessed using additional diagnostic imaging, including computed tomography (CT), positron emission tomography/computed tomography (PET/CT), and/or RAI WBS, to determine the

location and extent of suspected recurrence. Recurrence of disease was confirmed using imaging modalities and/or pathologic diagnosis with US-guided fine needle aspiration biopsy.

#### *TNM staging classification – 8th edition*

Medical charts and pathology reports of all patients were reviewed to re-classify patients based on the 7th and 8th editions of the AJCC/UICC TNM staging system. The age cutoff was increased from 45 years to 55 years. The biggest change in the T staging between the 7th and 8th edition is the definition of T3 disease. Minor ETE was removed. T3a is a new category and refers to a tumor >4 cm in the greatest diameter but limited to the thyroid gland. T3b is also a new category and is defined as a tumor of any size with gross ETE invading only the strap muscles. The definition of central neck lymph node (N1a) is changed to include both level VI and level VII compartments. However, there was no change in the N staging of all patients in our study, as patients with mediastinal lymph node metastasis underwent mRND owing to lateral lymph node metastasis.

#### *Statistical analysis*

Continuous, quantitative variables are presented as mean with standard deviation, whereas categorical and qualitative variables are reported as numbers with percentages. Student's *t* test, chi-square test, or Wilcoxon rank sum test was used for comparing groups. Univariate and multivariate Cox regression analyses were performed to identify the predictors of disease-free survival (DFS) and disease-specific survival (DSS) and to identify independent predictors of DFS and DSS. DFS and DSS were analyzed between the different groups with Kaplan–Meier analysis with log-rank test. A statistically significant difference was defined as  $p < 0.05$ .

To calculate the performance of each TNM staging, two statistical analyses were performed: the Harrell's c-index and time-dependent receiver operating characteristics (ROC) curve method. The time-dependent ROC curve method over the entire follow-up period was performed for calculating the Harrell's c-index and integrated area under the curve (iAUC): a higher iAUC indicates better predictive accuracy. Two-sided *p*-values of  $< 0.05$  were regarded as statistically significant.

Statistical analyses were performed using R package version 3.1.3 (<http://www.R-project.org>).

## Results

#### *Baseline clinicopathologic characteristics of study patients*

Supplementary Table S1 provides baseline clinicopathologic characteristics of 2294 patients with DTC. The mean age of patients was 45.8 years, and 2005 (87.4%) patients were women. Regarding age distribution, 1041 (45.4%) patients were aged <45 years, 777 (33.9%) were aged >45 and <55 years, and 476 (20.7%) were aged >55 years. The mean tumor size was 1.2 cm, and the majority (99.3%) were diagnosed as PTC. Multifocality and bilaterality of cancer were observed in 715 (31.2%) and 522 (22.8%) patients, respectively. A total of 1215 (68.1%) patients were pathologically diagnosed with ETE, with 971 (42.3%) having minimal ETE, 155 (6.8%) having invasion to the strap muscle, and 89 (3.9%) having invasion to the subcutaneous soft tissue, trachea, nerve, or esophagus. With respect to metastatic progression, 897 (39.1%) had pathologically confirmed central node metastasis, 322 (14.0%) had lateral node metastasis, and 35 (1.5%) had distant metastasis at the initial diagnosis. Overall, 1609 (70.1%) received postoperative RAI ablation. A total of 95 (4.1%) patients died, of whom 25 (1.1%) died of thyroid cancer, and recurrence was detected in 136 (5.9%) patients.

#### *Changes in T and TNM staging according to the 7th and 8th editions of the AJCC/UICC staging system*

Supplementary Table S2 provides distribution of the T, N, M, and TNM stage according to the 7th and 8th editions of the AJCC/UICC TNM staging system. According to the 7th edition, the number of patients with T1, T2, T3, and T4a was 1014 (44.2%), 56 (2.4%), 1135 (49.5%), and 89 (3.9%), respectively. Applying the 8th edition, the number of patients in each T stage changed to 1852 (80.7%), 178 (7.8%), 175 (7.7%), and 89 (3.9%), respectively. A notable finding in this study was that a significant number of T3 patients was reclassified as T1 (838, 36.5%) and T2 (122, 5.3%) patients (Table 1). Using the 7th edition, there were 1434 with stage I disease (62.5%), 17 with stage II (0.7%), 644 with stage III (28.1%), 176 with stage IVa (7.7%), and 23 with stage IVc disease (1.0%). After applying

**Table 1.** Migration number of patients based on the 7th and 8th editions of AJCC/UICC TNM staging system at the T stage.

T stage		8th edition			
		T1 (n = 1852)	T2 (n = 178)	T3 (n = 175)	T4 (n = 89)
7th edition	T1 (n = 1014)	1014	–	–	–
	T2 (n = 56)	–	56	–	–
	T3 (n = 1135)	838	122	175	–
	T4 (n = 89)	–	–	–	89

Data are expressed as patient numbers.  
AJCC, American Joint Committee on Cancer; TNM, tumor node metastasis; UICC, Union for International Cancer Control.

**Table 2.** Migration number of patients based on the 7th and 8th editions of AJCC/UICC TNM staging system at the TNM stage.

TNM stage		8th edition			
		I (n = 2058)	II (n = 186)	III (n = 33)	IV (n = 17)
7th edition	I (n = 1434)	1434	–	–	–
	II (n = 17)	5	12	–	–
	III (n = 644)	521	123	–	–
	IV (n = 199)	98	51	33	17

Data are expressed as patient numbers.  
AJCC, American Joint Committee on Cancer; TNM, tumor node metastasis; UICC, Union for International Cancer Control.

the 8th edition, the number at each stage was 2058 (89.7%), 186 (8.1%), 33 (1.4%), and 17 (0.7%), respectively. Table 2 shows changes in the number of patients according to the 7th and 8th AJCC/UICC TNM staging systems. As expected, there were significant changes in stage I, stage III, and stage IV. The number of stage I patients increased significantly from 1434 (62.5%) to 2058 (89.7%), whereas the number of stage III and IV patients significantly decreased from 644 (28.1%) to 33 (1.4%) and from 199 (8.7%) to 17 (0.7%), respectively.

#### *Risk factors for DFS with TNM staging system*

Recurrence was detected in 136 (5.9%) patients during the follow-up period. Univariate and multivariate analyses were performed with baseline clinicopathologic parameters to compare the accuracy of the two different TNM staging systems for prediction of recurrence. As a result, female sex, age, and advanced stage, especially stage III and IV in

the 8th edition, were verified as significant predictors for recurrence (Tables 3 and 4).

#### *Risk factors for DSS with TNM staging system*

A total of 25 (1.1%) patients died due to DTC during the follow-up period. To obtain the risk factors for DSS, univariate and multivariate analyses were performed with baseline clinicopathologic parameters to compare the accuracy of the two different TNM staging systems. Likewise, with DFS, female sex and advanced stage, especially with stage II, stage III, and stage IV in the 8th edition, were identified as significant predictors for DSS (Tables 4 and 5).

#### *Comparison of performance and predictive accuracy between the 7th and 8th editions of the AJCC/UICC TNM staging system*

Kaplan–Meier survival analyses were performed to compare the power to predict prognosis. There

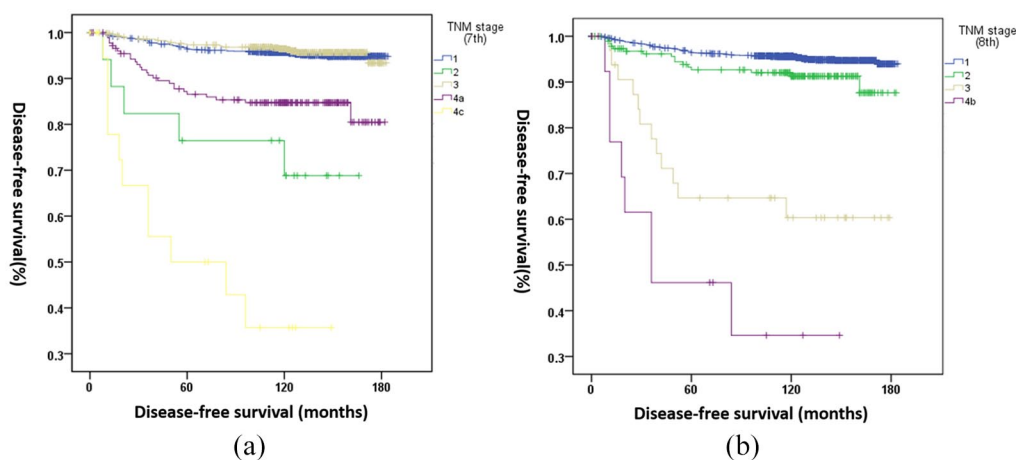
**Table 3.** Univariate and multivariate analysis of potential risk factors which influence on DFS.

Variables	Univariate		Multivariate	
	HR (95% CI)	<i>p</i> -value	HR (95% CI)	<i>p</i> -value
ETE				
No	Ref.			
Minimal	2.064 (1.358–3.136)	0.001		
Strap muscle	2.939 (1.577–5.477)	<0.001		
Soft tissue etc.	11.642 (6.983–19.411)	<0.001		
Female gender	2.711 (1.812–4.056)	<0.001	2.143 (1.388–3.310)	<0.001
Age (continuous variable)	1.006 (0.991–1.020)	0.440		
Age (≥45)	0.963 (0.688–1.349)	0.828		
Age (≥55)	1.344 (0.629–2.872)	0.445		
PTC ( <i>versus</i> FTC)	1.169 (0.163–8.359)	0.877		
Tumor size	1.852 (1.627–2.109)	<0.001		
CN metastasis	2.340 (1.581–3.464)	<0.001		
LN metastasis	3.171 (2.184–4.604)	<0.001		
Distant metastasis	17.850 (8.715–36.559)	<0.001		
7th edition				
I	Ref.		Ref.	
II	8.501 (2.911–24.827)	<0.001	6.735 (2.393–18.952)	<0.001
III	0.858 (0.540–1.363)	0.518	0.877 (0.547–1.407)	0.587
IVA	3.468 (2.263–5.880)	<0.001	2.323 (1.301–4.147)	0.004
IVC	22.443 (9.209–54.696)	<0.001	15.599 (4.062–59.903)	<0.001
8th edition				
I	Ref.		Ref.	
II	1.821 (1.051–3.158)	0.033	1.002 (0.506–1.983)	0.996
III	11.189 (5.353–23.384)	<0.001	4.570 (2.126–9.825)	<0.001
IVB	22.377 (7.956–62.937)	<0.001	1.349 (0.303–6.013)	0.694
Data are expressed as HR and 95% CI. A statistically significant difference was defined as <i>p</i> < 0.05. CI, confidence interval; CN, central nodes; DFS, disease-free survival; ETE, extrathyroidal extension; FTC, follicular thyroid cancer; HR, hazard ratio; LN, lateral nodes; PTC, papillary thyroid cancer; TNM, tumor node metastasis.				

**Table 4.** Multivariable cox proportional hazard model for DFS.

Variables	7th edition		8th edition	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Female gender	2.331 (1.586–3.247)	<0.001	2.474 (1.685–3.631)	<0.001
Age	1.006 (0.991–1.020)	0.440	1.129 (1.090–1.170)	<0.001
TNM stage				
I	Ref.		Ref.	
II	6.758 (2.715–16.818)	<0.001	1.932 (1.154–3.233)	0.012
III	0.879 (0.559–1.382)	0.576	9.995 (5.354–18.658)	<0.001
IVa	3.499 (2.236–5.473)	<0.001		
IVb			19.915 (9.603–41.301)	<0.001
IVc	19.208 (10.065–36.654)	<0.001		

Data are expressed as HR and 95% CI. A statistically significant difference was defined as  $p < 0.05$ . CI, confidence interval; CN, central nodes; DFS, disease-free survival; HR, hazard ratio; TNM, tumor node metastasis.

**Figure 1.** Disease-free survival curves according to the (a) 7th or (b) 8th edition of the AJCC/UICC TNM staging system.

AJCC, American Joint Committee on Cancer; TNM, tumor node metastasis; UICC, Union for International Cancer Control.

were significant differences in DFS between the two TNM staging systems (log-rank test,  $p < 0.001$ ; Figure 1). The notable result to emerge from the results depicted in Figure 1 is that DFS was significantly better reflected when the 8th edition was applied rather than the 7th edition. To investigate the prediction of recurrence between the 7th and 8th editions, Harrell's c-index and iAUC were calculated with the two different TNM staging systems (Table 7). Using Harrell's

c-index and iAUC, the discriminatory ability of each TNM staging system was 0.639 and 0.657, and 0.637 and 0.658 for the 7th and the 8th editions of the AJCC/UICC TNM staging systems, respectively. Thus, the 8th edition had greater power to predict recurrence than the 7th edition.

In the same manner with DFS, the same statistical methods were used to analyze DSS of the two different TNM staging systems. There were



**Table 5.** Univariate and multivariate analysis of potential risk factors which influence on DSS.

Variables	Univariate		Multivariate	
	HR (95% CI)	<i>p</i> -value	HR (95% CI)	<i>p</i> -value
ETE				
No	Ref.			
Minimal	1.201 (0.268–5.378)	0.811		
Strap muscle	0.112 (0.030–0.420)	0.001		
Soft tissue and etc.	0.020 (0.006–0.062)	<0.001		
Female gender	5.726 (2.423–11.490)	<0.001	3.308 (1.476–7.416)	0.004
Age (continuous variable)	1.129 (1.090–1.170)	<0.001	1.079 (1.023–1.137)	0.005
Age (≥45)	21.634 (2.931–159.674)	0.003		
Age (≥55)	9.086 (3.950–20.899)	<0.001		
PTC (versus FTC)	13.195 (3.115–55.897)	<0.001		
Tumor size	0.380 (0.302–0.479)	<0.001		
CN metastasis	4.208 (1.769–10.009)	0.001		
LN metastasis	10.101 (4.583–22.261)	<0.001		
Distant metastasis	26.159 (10.486–65.259)	<0.001		
7th edition				
I+II	Ref.		Ref.	
III	4.594 (0.417–50.661)	0.213	1.579 (0.118–21.117)	0.730
IV	175.685 (23.678–1303.535)	<0.001	23.835 (2.345–242.308)	0.007
8th edition				
I	Ref.		Ref.	
II	23.693 (7.134–78.690)	<0.001	4.887 (1.046–22.833)	0.044
III	125–986 (36.833–430.931)	<0.001	8.149 (1.587–41.847)	0.012
IVb	272–988 (76.835–969.899)	<0.001	10.014 (1.563–64.183)	0.015
Data are expressed as HR and 95% CI. A statistically significant difference was defined as $p < 0.05$ . CI, confidence interval; CN, central nodes; DSS, disease-specific survival; ETE, extrathyroidal extension; FTC, follicular thyroid cancer; HR, hazard ratio; LN, lateral nodes; PTC, papillary thyroid cancer; TNM, tumor node metastasis.				

significant differences in DSS (log-rank test,  $p < 0.001$ ; Figure 2). Harrell's *c*-index was 0.929 and 0.948, and iAUC were 0.921 and 0.954,

respectively (Table 7). The 8th edition is, thus, more accurate for the prediction of DSS than the 7th edition.

**Table 6.** Multivariable cox proportional hazard model for DSS.

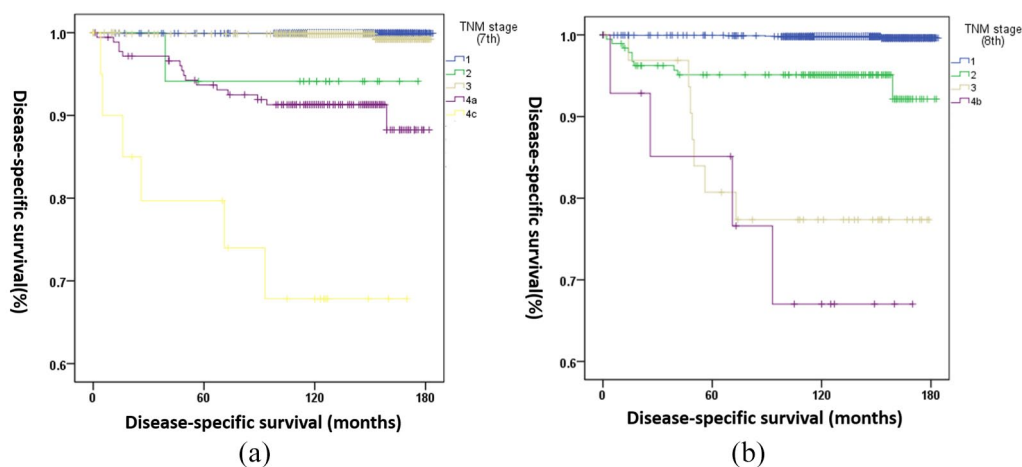
Variables	7th edition		8th edition	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Female gender	3.53 (0.283–1.588)	0.002	3.385 (0.295–1.494)	0.003
Age	1.098 (0.911–1.052)	<0.001	1.044 (0.958–0.99)	0.113
TNM stage				
I	Ref.		Ref.	
II			13.004 (0.077–3.243)	<0.001
III	1.631 (0.613–0.144)	0.692	64.672 (0.015–14.742)	<0.001
IV	48.586 (0.021–6.273)	<0.001		
IVb			57.664 (0.017–10.286)	<0.001

Data are expressed as HR and 95% CI. A statistically significant difference was defined as  $p < 0.05$ . CI, confidence interval; DSS, disease-specific survival; HR, hazard ratio; TNM, tumor node metastasis.

**Table 7.** Comparison of the performance and predictive accuracy between the 7th and 8th editions of AJCC/UICC TNM staging system.

Method	Outcome	7th edition	8th edition
Harrel's c-index	DFS	0.639	0.657
	DSS	0.929	0.948
iAUC	DFS	0.637	0.658
	DSS	0.921	0.954

AJCC, American Joint Committee on Cancer; DFS, disease-free survival; DSS, disease-specific survival; iAUC, integrated area under the curve; TNM, tumor node metastasis; UICC, Union for International Cancer Control.



**Figure 2.** Disease-specific survival curves according to (a) the 7th or (b) 8th edition of the AJCC/UICC TNM staging system. AJCC, American Joint Committee on Cancer; TNM, tumor node metastasis; UICC, Union for International Cancer Control.



## Discussion

The AJCC/UICC TNM staging is the most basic and widely used cancer staging system owing to its accuracy for predicting prognosis and survival.<sup>14,15</sup> For thyroid cancer, this staging system is the first systematic risk stratification that patients undergo at the time of diagnosis.<sup>16</sup> The AJCC/UICC periodically revises the TNM staging system to improve its predictability of prognosis and reflect the newly acquired clinical data.<sup>14,15</sup> From January 2018, the 8th edition of the AJCC/UICC TNM staging system has been applied, and it includes a few major changes for thyroid cancer, including cutoff age at diagnosis, new T and N classification, and stage categories according to the revised TNM staging system. In our study, we compared the 7th and 8th editions of the AJCC/UICC TNM staging system for 2294 patients with DTC. Among the total, 36.2% of patients were restaged to lower TNM stages, and 41.8% with T3 classification were reclassified into T1 or T2 when we applied the 8th edition. The Kaplan–Meier curves for DFS and DSS were both significantly better reflected when the 8th edition was applied than the 7th edition. Values of the Harrell's c-index and iAUC were higher in the 8th edition than in the 7th edition. These results suggest that the 8th edition has more power in predicting prognoses than the 7th edition.

Modification of the age cutoff point from 45 to 55 is a major change in the 8th edition of the AJCC/UICC TNM staging system. For thyroid cancer, age at the time of diagnosis is a significant independent predictor of prognosis and mortality.<sup>17,18</sup> The mortality of thyroid cancer increased progressively with advancing age.<sup>19,20</sup> Since the 2nd edition of the AJCC/UICC TNM staging system was published in 1983, the cutoff age of 45 years has been used as a non-anatomic variable for DTC staging.<sup>21,22</sup> Recent studies have suggested that a cutoff age of 45 years can statistically lead to over-staging in a notable number of patients.<sup>8,15,19,23,24</sup> Reflecting these studies, the age cutoff point in the 8th edition of the AJCC/UICC TNM staging guidelines was changed from 45 to 55 years. It was suggested that patients aged between 45 and 55 years without distant metastasis at the time of diagnosis be re-categorized to stage I. Upon the application of the new cutoff age, 777 patients (33.9%) were between 45 and 55 years of age, and their TNM stages were reclassified as stage I or II in our study.

Another significant change in the 8th edition is the definition of the T classification of thyroid cancer,<sup>15</sup> especially the meaning of ETE in T3 stage was changed to 'gross ETE invading only strap muscles', whereas it meant 'minimal ETE to the sternothyroid muscle or perithyroidal soft tissue' in the 7th edition.<sup>15</sup> Therefore, T3 is defined as the presence of gross ETE invading the strap muscle in the 8th edition if the primary tumor size of DTC is  $\leq 4$  cm.<sup>22</sup> Previous studies have demonstrated that gross ETE is highly associated with worse survival in patients with DTC.<sup>25,26</sup> However, minor extension, such as capsule invasion observed on histologic examination, is not clinically appreciated in the 8th edition, as increasing evidence has shown that minor ETE lacks a prognostic value for persistent/recurrent disease and DSS and recurrence-free survival.<sup>13,15,27,28</sup> In this study, 41.8% of patients with T3 classification by the 7th edition were reclassified as T1 or T2 according to the 8th edition.

In our study, the prognosis of patients with DTC showed more regular distribution with the 8th edition than with the 7th edition on Kaplan–Meier curves. When the 7th edition was applied, patients in stage I and III exhibited similar DFS and DSS and stage II presented worse prognosis than both stages I and III; stage II even suggested poorer DFS than stage IV when using the 7th edition. However, the Kaplan–Meier curves for DFS and DSS with the 8th edition appeared to be more reasonable, showing, in serial order, from the best prognosis in stage I to the worst prognosis in stage IV. Considering these aspects and higher values of the Harrell's c-index and iAUC for DFS and DSS, the 8th edition presents more exquisite risk stratification for patients with DTC than the 7th edition. Clinical benefits could be expected as it can provide adequate impression for the treatment strategy for patients with DTC.

This present study has some limitations. The most important limitation is that this study was designed retrospectively. In addition, there is a possibility of selection bias, because all enrolled patients were from a single tertiary institution. Meanwhile, the follow-up period is relatively short ( $132.9 \pm 27.9$  months), and the DSS rate was too low to allow significant statistical analysis. A longer follow-up period is necessary to predict prognosis of patients with DTC because DTC is characterized by indolent features.

## Conclusion

To the best of our knowledge, only a few studies have compared the 7th and 8th editions of the AJCC/UICC TNM staging system. A significant population was shown as migrating into down-staging after applying the 8th edition of the AJCC/UICC TNM staging system, which provided significantly better accuracy in predicting DFS and DSS in patients with DTC. Further research should be undertaken to validate our results.

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## Author contributions

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**Jin Kyong Kim:** Data curation; Formal analysis; Software; Writing – original draft

**Cho Rok Lee:** Conceptualization; Data curation; Formal analysis; Writing – review and editing

**Sang-Wook Kang:** Conceptualization; Writing – review and editing

**Jandee Lee:** Methodology; Resources; Writing – review and editing

**Jong Ju Jeong:** Methodology; Resources; Writing – review and editing

**Kee-Hyun Nam:** Investigation; Writing – review and editing

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The authors declare that there is no conflict of interest.

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## Supplemental material

Supplemental material for this article is available online.

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