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PROGNOSTIC SIGNIFICANCE OF SUBDIVISION OF N FACTOR AMONG PAPILLARY THYROID CANCER WITH N1

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Introduction

・In the 9th edition of general rules for the description of thyroid cancer (GRDTC), published in October 2023, the N factor is subdivided according to the maximum diameter of metastatic lymph node, the presence of extra-nodal extension (ENE), and the location of mediastinal lymph node (Level VII)

・This study aimed to investigate the clinical usefulness and outcomes in the papillary thyroid carcinoma (PTC) patients with lymph node metastasis risk-stratified according to the 9th edition of GRDTC.

Materials and Methods

Study participants: A total of 703 patients with PTC who underwent initial thyroidectomy at our institution between January 2000 and October 2023 were included.

Definitions: N factor was subdivided according to the maximum diameter of metastatic lymph node, the presence of ENE, and the location of mediastinal lymph node in the 9th edition of GRDTC (Table 1)

Outcomes: Cause-specific survival (CSS) and Disease-free survival (DFS) were assessed by the N factor according to the 9th edition of GRDTC.

Table 1. 9th edition of GRDTC

pN1a	Metastasis to level VI or VII
pN1a-1	Lymph node metastasis ≤3 cm and the absence of extra-nodal extension
pN1a-2	Lymph node metastasis >3 cm or the presence of extra-nodal extension
pN1a-3	XIIb metastasis
pN1b	Metastasis to unilateral, bilateral or contralateral lateral neck lymph nodes (levels I, II, III, IV or V)
pN1b-1	Lymph node metastasis ≤3 cm and the absence of extra-nodal extension
pN1b-2	Lymph node metastasis >3 cm or the presence of extra-nodal extension
Level VII (XI)	Lymph nodes under the suprasternal notch
XIIa	From the suprasternal notch to the cranial end of innominate vein
XIIb	Under the cranial end of innominate vein

Results

・The baseline characteristics are shown in Table 2.

Table 2. Baseline characteristics

	N = 703
Sex	
Male / Female	193 (27%) / 510 (73%)
Age (years)	
<55 / ≥55	368 (52%) / 335 (48%)
Extent of thyroidectomy	
Total / Lobectomy	321 (46%) / 382 (54%)
Lymph node dissection	
Central / Lateral	364 (52%) / 339 (48%)
TNM classification	
≤pT2 / ≥pT3	445 (72%) / 172 (28%)
pN1a-1 / 1a-2 / 1a-3 /1b-1 / 1b-2	383 (54%) / 13 (2%) / 0 / 234 (33%) / 73 (10%)
pM0 / M1	664 (94%) / 39 (6%)

Clinical outcome

・Among the 703 patients with PTC, the 10-year CSS rates of patients with pN1a-1 (n = 383), pN1a-2 (n = 13), pN1b-1 (n = 234), and pN1b-2 (n = 73) were 97.9%, 100%, 95.4%, and 76.2%, respectively ($p < 0.001$) (Figure 1).

・Among the 664 patients with M0 PTC, the 10-year DFS rates of patients with pN1a-1 (n = 378), pN1a-2 (n = 13), pN1b-1 (n = 215), and pN1b-2 (n = 58) were 86.9%, 62.5%, 79.9%, and 59.4%, respectively ($p < 0.001$) (Figure 2).

Analyses of prognostic factors for CSS and DFS

・Among the 703 patients with PTC, multivariate analysis was performed by including age, T factor, N factor, pN1a/1b-2, and M1, and identified age ≥55 years (HR = 11.220, 95% CI [(2.576–48.830], p = 0.001), T factor (≥T3) (HR = 4.938, 95% CI [1.904–12.810], p = 0.001), pN1a/1b-2 (HR = 3.032, 95% CI [1.172–7.844], p = 0.022), and M1 (HR = 2.543, 95% CI [1.005–6.432] as independent negative prognostic factors for CSS.

・Among the 664 patients with M0 PTC, multivariate analysis was performed by including sex, age, T factor, N factor, and pN1a/1b-2, and identified sex (HR = 1.630, 95% CI [1.049–2.533], p = 0.030), age ≥55 years (HR = 2.200, 95% CI [1.405–3.444], p < 0.001), N factor (HR = 1.620, 95% CI [1.016–2.582], p = 0.043), and pN1a/b-2 (HR = 2.680, 95% CI [1.520–4.726], p < 0.001) as independent negative prognostic factors for DFS.

Figure 1. Cause-specific survival

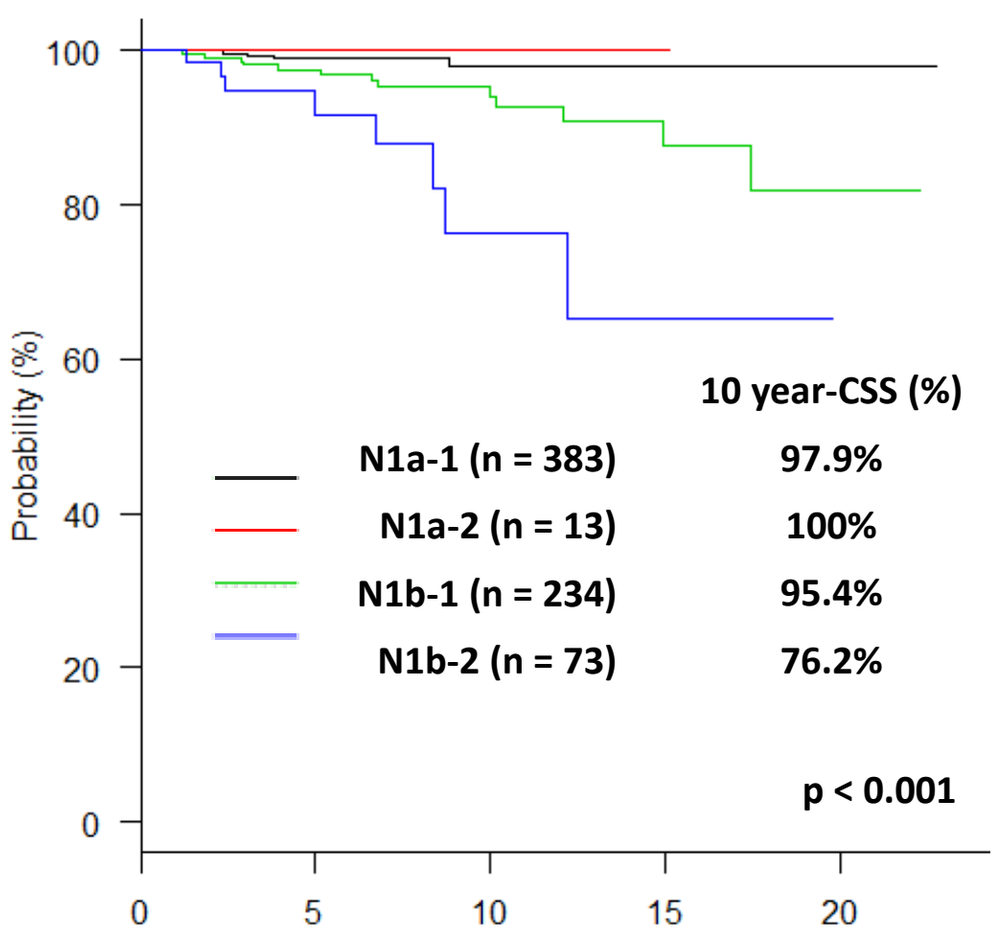
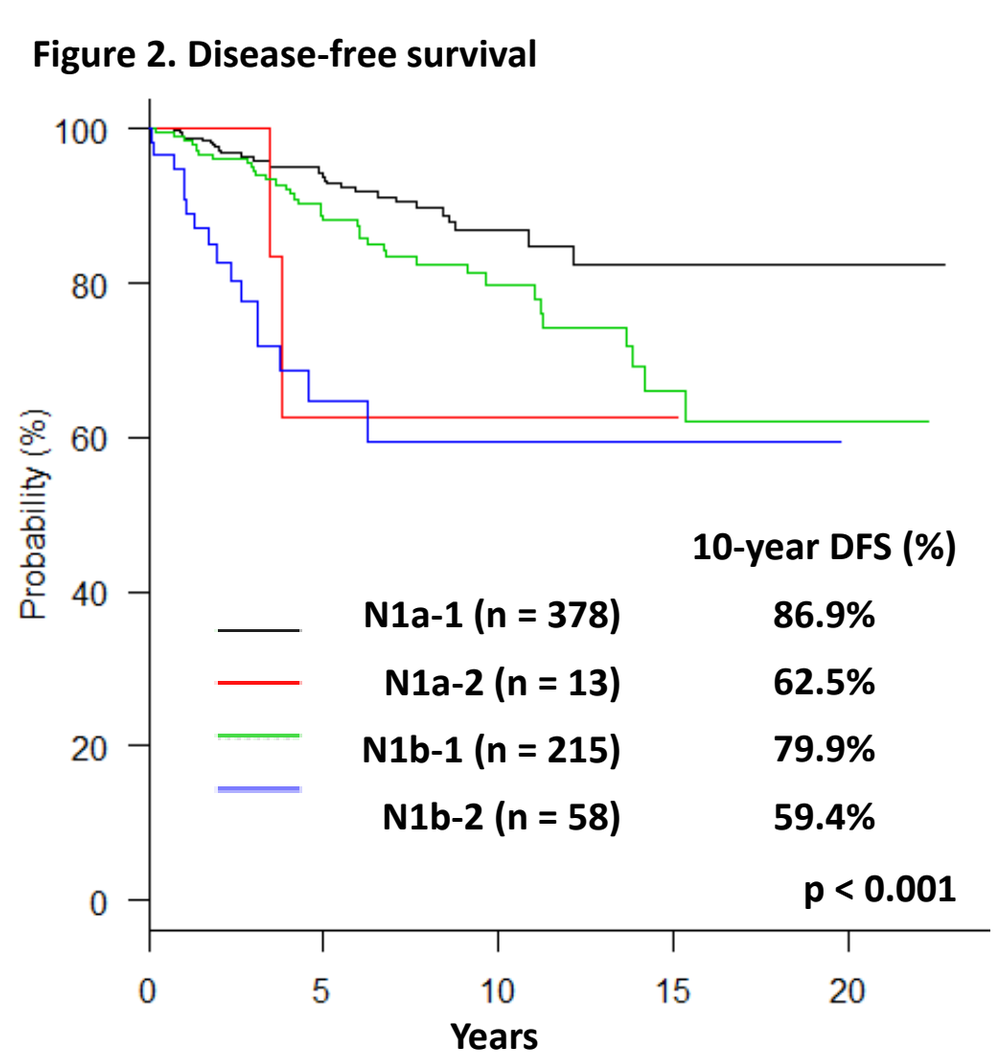


Figure 2. Disease-free survival



Discussion

・Sugitani et al. revealed that the large (3 cm or larger) nodal metastasis was the independent factor for disease-specific death (Risk ratio = 5.3, 95% CI [2.0-14.2], p = 0.0009) and DFS (Risk ratio = 2.9, 95% CI [1.3-6.2], p = 0.0078).

・Veronese et al. revealed that the presence of ENE status carried a significantly higher risk of all-cause (HR = 3.21, 95% CI [2.25–4.59], p < 0.0001) and cancer-specific mortality (HR = 3.00, 95% CI [1.37–6.57], p = 0.006) and disease recurrence (HR = 1.55, 95% CI [1.22–1.97], p < 0.0001).

・Our study results demonstrated that lymph node size and ENE were prognostic factors as well as previous studies.

・The 9th edition of GRDTC can identify PTC patients with poorer prognosis. Furthermore, it will lead to appropriate selection of additional postoperative treatment such as adjuvant radioactive iodine therapy.

Conclusion

The factor of N1a/1b-2 was the independent prognostic factor for CSS and DFS. Therefore, the 9th edition of GRDTC may be useful to stratify the prognosis of PTC patients.

References
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