SUBSET ANALYSIS OF THE JAPANESE RISK CLASSIFICATION GUIDELINES FOR PAPILLARY THYROID CARCINOMA

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Abstract. Guidelines published by the Japan Association of Endocrine Surgeons (JAES)/Japanese Society of Thyroid Surgery (JSTS) for patients with papillary thyroid carcinoma describe four risk classes (very low-, low-, intermediate- and high-risk) for deciding on therapeutic strategies. Here, we investigate cause-specific survival (CSS) of high- and intermediate-risk patients, taking their age into consideration. CSS of intermediate-risk patients ≥55 years was poorer than that of those <55 years (p < 0.0001) (20-year CSS rates, 96.9% vs. 98.7%). CSS of intermediate-risk patients <55 years was excellent but still poorer (p = 0.0152) than that of low- or very low-risk patients (20-year CSS rates, 100%). CSS of high-risk patients <55 years (20-year CSS rates, 96.0%) was similar (p = 0.7412) to that of intermediate-risk patients ≥55 years, while high-risk patients ≥55 years (20-year CSS rates, 80.6%) showed much poorer prognosis (p < 0.0001) than the others. In high-risk patients <55 years, distant metastasis (M1), extrathyroid extension (Ex), node metastasis ≥3 cm, and extranodal tumor extension, and in those ≥55 years, M1, Ex, and tumor size >4 cm were regarded as prognostic factors on multivariate analysis. We therefore conclude that 1) prognosis of high-risk patients ≥55 years should be carefully treated because of significantly poor prognosis, 2) prognostic factors of high-risk patients vary according to patient age, and 3) overtreatment of intermediate-risk patients and young high-risk patients should be avoided; however, appropriate treatment strategies need to be established, considering that their prognoses are excellent, but still poorer than low- or very low-risk patients.

Key words: Papillary thyroid carcinoma, Guidelines, Prognosis, Age, Extrathyroid extension

PAPILLARY THYROID CARCINOMA (PTC) is generally an indolent disease. However, PTCs have some aggressive clinicopathological characteristics, which are associated with a poor prognosis. To date, there are several classification systems for differentiated thyroid carcinoma (DTC), including PTC, such as the TNM staging system [1], AMES (age, metastases, extent, size) [2] and the MACIS (distant Metastasis, patient Age, Completeness of resection, local Invasion, and tumor Size) scoring system [3], in addition to the guidelines developed by the American Thyroid Association (ATA) which utilize the individual risk classification of DTC [4].

In Japan, guidelines established by the Japan Association of Endocrine Surgeons (JAES)/Japanese Society of Thyroid Surgery (JSTS) (the current Japan Association of Endocrine Surgery) also proposed utilizing the risk classification for PTC, which is graded as: 1) very low-risk, tumor size (T) ≤1 cm without clinical lymph node or distant metastasis; 2) low-risk, T measuring 1.1–2 cm without lymph node or distant metastasis; 3) high-risk, PTC including at least one of the following characteristics, clinical distant metastasis-positive (M1), T >4 cm, clinical lymph node metastasis (N) >3 cm (N2), extrathyroid extension (Ex) and extranodal tumor extension (LNEt) based on intraoperative findings, and; 4) intermediate-risk, PTC not belonging to other categories [5]. The Japanese guidelines recommend various therapeutic strategies according to patients’ risks, which extend to thyroidectomy, ranges of node dissection, and administration of adjuvant or therapeutic radioactive iodine (RAI) therapy.

However, there is still uncertainty regarding whether risk classification guidelines accurately reflect the prognoses of patients with PTC. We previously showed that, although very-low and low-risk patients had an excellent prognosis regardless of patient age, older patients with intermediate-risk and those with high-risk had significantly poorer prognoses than young patients with these risks [6].

In this study, we compared the prognoses of four cate-
gories, old high-risk patients, young high-risk patients, old intermediate-risk patients, and young intermediate-risk patients and investigated whether therapeutic strategies in high-risk and intermediate-risk patients should vary according to the patient age.

Patients and Methods

Patients
We enrolled 1,254 high-risk and 1,774 intermediate-risk patients with PTC according to the criteria outlined in the Japanese guidelines [5] mentioned above. For comparing investigation, we also enrolled 2,652 low-risk or very low-risk patients. Participants underwent local curative surgery between February 1988 and January 2015 at Kuma Hospital, and all patients were diagnosed as having PTC based on a postoperative pathological examination. Tumor size (T) and lymph node metastasis (N) were evaluated in preoperative imaging studies. Extrathyroid extension (Ex) and extranodal tumor extension (LNEx) were evaluated based on intraoperative findings. We did not enroll T4b cases, as the number of these cases was small. We divided Ex corresponding to T4a into two categories as previously described [7]; in T4a1 the tumors extended to the tracheal adventitia and cartilage, esophageal muscle layer, recurrent laryngeal nerve, and cricothyroid and inferior constrictor muscles, and in T4a2, the tumors extended to other organs such as the subcutaneous soft tissues, thyroid cartilage, larynx, tracheal mucosa, esophageal mucosa, jugular and brachiocephalic veins, and sternocleidomastoid muscle. These categories were created because the prognosis for those with T4a2 versus T4a1 patients differs significantly as demonstrated in our earlier study [7]. Regarding T3b (extension to the strap muscles), we did not classify this as Ex-positive; patients with T3b without high-risk features were categorized as intermediate-risk in this study. We divided LNEx into two categories, LNEx2 and LNEx1, based on the organs to which metastatic nodes invaded corresponding to T4a1 and T4a2; we then compared the prognoses between the two groups. However, we have subsequently found that the difference in prognoses between LNEx2 and LNEx1 did not differ [8]. In light of this, we analyzed LNEx as a single group for the present study.

We excluded patients who had other thyroid malignancies such as anaplastic, medullary, or follicular carcinomas or malignant lymphoma. Additionally, we excluded patients whose operation and pathological reports were inadequate for accurate classification based on the risk classifications.

Patient ages ranged from 7–89 years (median 49 years); there were 2,570 females and 458 males.

Surgical designs
Total thyroidectomy was performed for 938 (77.5%) high-risk and 976 (54.3%) intermediate-risk patients. The remaining patients underwent other types of thyroidectomies such as subtotal thyroidectomy, lobectomy with isthmectomy and isthmectomy. Therapeutic or prophylactic central node dissection was performed for 1,173 high-risk patients (95.4%), and for 1,725 intermediate-risk patients (90.2%). Prophylactic or therapeutic, unilateral or bilateral modified radical neck dissection was performed 1,124 high-risk patients (91.4%) and 1,623 intermediate-risk patients (90.2%). Ten patients with high-risk and three with intermediate-risk PTC also underwent therapeutic upper mediastinal dissection. Table 1 summarizes the backgrounds, clinical features, and therapeutic strategies for high- and intermediate-risk patients.

Postoperative follow-up
Seventy-five patients (53 in high- and 22 in intermediate-risk groups) were administrated radioactive iodine (RAI) (≥30 mCi) after total thyroidectomy either for ablation of the remnant thyroid or adjuvant therapy (Table 1). Of the 66 M1 patients, 46 underwent RAI therapy (≥100 mCi) at least one time, but the remaining 20 did not undergo RAI therapy because of old age and/or poor condition.

All patients were followed-up with blood examinations and imaging studies such as an ultrasound performed 1–2 times per year. Chest roentogenography, a computerized tomography (CT) scan, and bone scintigraphy were also used for follow-up assessments at each physician’s discretion. The follow-up periods ranged from 6–357 months (median 176 months).

We requested review to the ethical committee; however, approval was not required due to the retrospective nature of the study.

Statistical analyses
The Kaplan-Meier method with log-rank tests was utilized using software StatView statistical software. We employed Cox-hazard proportion models for multivariate analyses. P-values <0.05 were adopted as statistically significant and 0.05 ≤p<0.1 were regarded as marginally significant. For multivariate analysis, we included factors with a statistically significant or marginally significant prognostic value on univariate analysis.

Results
Of the 1,230 high-risk patients, M1, T4a2, T4a1, T >4 cm, N2, and LNEx were detected in 66 (5.4%), 112 (9.1%), 594 (48.3%), 558 (45.4%), 192 (15.6%), and 128
Table 1  Backgrounds and clinicopathological features of high- and intermediate-risk patients.

a) High-risk patients (1,230 patients)

| Variables        | Patients’ numbers (%) |
|------------------|------------------------|
| Age              |                        |
| ≥55 years        | 586 (47.6%)            |
| <55 years        | 644 (52.4%)            |
| Tumor size       |                        |
| >4 cm            | 558 (45.4%)            |
| ≤4 cm            | 672 (54.6%)            |
| T factor         |                        |
| T4a2             | 112 (9.1%)             |
| T4a1             | 594 (48.3%)            |
| T1-T3a           | 524 (42.6%)            |
| N factor         |                        |
| N2               | 192 (15.6%)            |
| N1               | 389 (31.6%)            |
| N0               | 649 (52.8%)            |
| M factor         |                        |
| M1               | 66 (5.4%)              |
| M0               | 1,164 (94.6%)          |
| LNEx             |                        |
| Positive         | 128 (10.4%)            |
| Negative         | 1,102 (89.6%)          |
| Thyroidectomy    |                        |
| Total            | 938 (77.5%)            |
| Non-total        | 272 (22.5%)            |
| Lymph node dissection |                    |
| None             | 57 (4.6%)              |
| Central only     | 49(4.0%)               |
| Central + lateral| 1,124(91.4%)           |
| RAI administration|                       |
| (≥30 mCi)        |                        |
| Yes              | 993(8.0%)              |
| No               | 1,131(92.0%)           |

1) One patient underwent upper mediastinal dissection also.
2) Nine patients underwent upper mediastinal dissection also.
3) Including RAI therapy for 46 M1 patients.

Abbreviations, RAI, radioactive iodine

b) Intermediate-risk patients (1,798 patients)

| Variables        | Number of patients (%) |
|------------------|------------------------|
| Age              |                        |
| ≥55 years        | 574 (31.9%)            |
| <55 years        | 1,234 (68.1%)          |
| Tumor size       |                        |
| 2.1–4 cm         | 1,410 (78.4%)          |
| ≤2 cm            | 388 (21.6%)            |
| N factor         |                        |
| N1               | 638 (35.5%)            |
| N0               | 1,160 (64.5%)          |
| Thyroidectomy    |                        |
| Total            | 976 (54.3%)            |
| Non-total        | 822 (45.7%)            |
| Lymph node dissection |                    |
| None             | 73 (4.1%)              |
| Central only     | 102 (5.7%)             |
| Central + lateral| 1,623(90.2%)           |
| RAI therapy      |                        |
| (≥30 mCi)        |                       |
| Yes              | 22 (1.2%)              |
| No               | 1,776 (98.8%)          |

1) Three patients underwent upper mediastinal dissection also.
2) Ablation or adjuvant therapy

Abbreviations, RAI, radioactive iodine

patients (10.4%), respectively (Table 1). Of these, 644 (52.4%) were younger than 55 years and the remaining 586 (47.6%) were aged at 55 years or older (Table 1). Of the 1,798 intermediate-risk patients, 638 (35.5%) were classified as N1 and 1,410 (78.4%) had PTC measuring 2.1–4 cm. Twenty-four patients (1.3%) were classified as T3b. Five-hundred and seventy-four (31.9%) were younger than 55 years and the remaining 1,224 (68.1%) were aged 55 years or older (Table 1).

To date, 94 (7.6%) of the high-risk patients and 18 (1.0%) of the intermediate-risk patients have died from thyroid carcinoma. For low- or very-low risk patients, only two (0.1%) have died of thyroid carcinoma. Fig. 1 shows the Kaplan-Meier curves of CSS for high-risk and intermediate-risk patients. CSS of high-risk patients was significantly poorer than that for intermediate-risk patients (10- and 20-year CSS rates 92.9% and 89.7%, vs. 99.6% and 98.5%, respectively, p < 0.0001). Since only two patients died of thyroid carcinoma, 10- and 20-year CSS rates of low- or very low-risk patients were 100% and 100%, respectively, after rounding off to the nearest hundredths place and CSS was significantly better than those of the other groups (p < 0.0001). The univariate analysis for high-risk patients showed that M1 (p < 0.0001), age ≥55 years (p < 0.0001), T4a2 (p < 0.0001), N2 (p < 0.0001), LNEx (p = 0.0002), and non-total thyroidectomy (p = 0.0101) had prognostic value, but T >4 cm (p = 0.6362) and T4a (p = 0.4863) did not. Table 2 shows the results of the multivariate analyses for CSS of high-risk patients. In high-risk cases, M1 (p < 0.0001, hazard ratio [HR] = 8.403), T4a2 (p < 0.0001, HR = 3.559), age ≥55 years (p < 0.0001, HR = 6.757), N2 (p < 0.0001, HR = 2.193), and non-total thyroidectomy (p = 0.0493, HR = 1.848) were recognized as prognostic factors.

Next, we set the age cut off at 55 years and the patients were classified based on TNM [1]; we subsequently compared the CSS of high-risk patients ≥55 years and <55 years, and intermediate-risk patients ≥55 years and <55 years. Fig. 2 shows the Kaplan-Meier curves of four subsets of CSS. Ten- and 20-year CSS rates were 98.9% and 96.0% for high-risk patients <55 years old, 90.7% and 80.6% for high-risk patients ≥55 years, 99.8% and 98.7% for intermediate-risk patients <55 years, and 99.1% and 96.9% for intermediate-risk patients ≥55 years, respectively. CSS of intermediate-risk and high-risk patients ≥55 years old was significantly poorer (p < 0.0001) compared with those aged <55 years. Furthermore, CSS of intermediate-risk patients ≥55 years did not significantly differ from that of high-risk patients <55 years (p = 0.7412). The CSS of intermediate patients <55 years was excellent; however, it was significantly poorer (p = 0.0152) than that of low- or very low-risk patients.
In the subset of high-risk patients <55 years, univariate analysis indicated that, M1 ($p < 0.0001$), T4a2 ($p < 0.0001$), N2 ($p < 0.0001$), and LNEx ($p < 0.0001$) had prognostic value. Non-total thyroidectomy had a marginal prognostic significance ($p = 0.0614$), but T >4 cm ($p = 0.4592$) and T4a1 ($p = 0.6519$) did not. From the multivariate analyses, the HR for M1 was highest at 8.850 ($p < 0.0001$), followed by T4a2 ($p = 0.0012$, HR = 7.092), N2 ($p = 0.0022$, HR = 4.739), and LNEx ($p = 0.0155$, HR = 3.831). Non-total thyroidectomy was not regarded as prognostically significant on multivariate analysis ($p = 0.6314$, HR = 1.669) (Table 3). In high-risk patients aged ≥55 years, all factors including M1 ($p < 0.0001$), T4a2 ($p < 0.0001$), N2 ($p = 0.0005$), LNEx ($p = 0.0161$), T >4 cm ($p = 0.0159$) and T4a1 ($p = 0.0177$) significantly affected CSS of patients in univariate analyses. Non-total thyroidectomy had a marginal significance ($p = 0.0534$). From the multivariate analysis, M1 was the most significant prognostic factor ($p < 0.0001$, HR = 14.493). T4a2 had a significant prognostic value ($p < 0.0001$, HR = 4.975) (Table 4), similar to the subset of patients aged <55 years. However, in contrast to younger patients, N2 had only a marginal prognostic value ($p = 0.0500$, HR = 1.992), and LNEx was not recognized as a prognostic factor ($p = 0.2828$, HR = 1.555). Instead, T >4 cm ($p < 0.0001$, HR = 3.226), and T4a1 ($p = 0.0177$, HR = 2.387) affected CSS of patients. Non-total thyroidectomy did not affect patient prognosis on multivariate analysis ($p = 0.1612$, HR = 1.605).

| Variables                  | Univariate analysis | Multivariate analysis | HR (95% CI)     |
|----------------------------|---------------------|-----------------------|-----------------|
| Age ≥55 yrs                | <0.0001             | <0.0001               | 6.757 (3.937–11.628) |
| M1                         | <0.0001             | <0.0001               | 8.403 (5.076–14.085) |
| T4a2                       | <0.0001             | <0.0001               | 3.559 (2.247–5.650) |
| N2                         | <0.0001             | 0.0031                | 2.193 (1.304–3.690) |
| Non-total thyroidectomy    | 0.0101              | 0.0493                | 1.848 (1.010–3.412) |
| LNEx                       | 0.0002              | 0.0979                | 1.618 (0.915–2.857) |

Independent prognostic factors are highlighted in bold.

T, tumor size; N2, N ≥3 cm; LNEx, extranodal tumor extension; HR, Hazard ratio; CI, confidence interval
In this study, we demonstrated that: 1) CSS of high-risk patients ≥55 years was significantly poorer than other patients; 2) CSS of high-risk patients <55 years was similar to that of intermediate-risk patients ≥55 years; 3) CSS of intermediate-risk patients <55 years was excellent, but was still poorer than that of low- and very low-risk patients; 4) M1 and T4a2 significantly affected the CSS of high-risk patients regardless of patient age; and 5) N2 and LNEx had significant prognostic values for high-risk patients ≥55 years, while T4a1 and T >4 cm had strong prognostic impact for those <55 years.

To date, many studies have been published regarding prognostic factors of high-risk patients. Sugitani et al. demonstrated that, for young patients, M1 was the only significant risk factor for young patients aged <50 years [9]. We recently analyzed patients <55 years and showed that, other than M1, N2 and T4a2 significantly affected CSS of patients [7]. The reason for the discrepancy remains unclear, but our series enrolled a larger number of patients and the follow-up period was longer than Sugitani’s study, which may partially explain the discrepancy. For patients ≥50 years, they identified M1, T4a1 or T4a2, and N2 as risk factors for poor prognosis.

**Discussion**

![Kaplan-Meier curves for CSS of the intermediate- and high-risk patients aged <55 years and ≥55 years](image)

**Table 3** Univariate and multivariate analyses for prognostic factors in high-risk patients aged <55 years

| Variables                  | Univariate analysis | Multivariate analysis | HR (95% CI)     |
|----------------------------|---------------------|-----------------------|-----------------|
| M1                         | <0.0001             | 0.0001                | 8.850 (2.907–27.027) |
| T4a2                       | <0.0001             | 0.0012                | 7.092 (2.174–23.256) |
| N2                         | <0.0001             | 0.0022                | 4.739 (1.748–12.821) |
| LNEx                       | <0.0001             | 0.0155                | 3.831 (1.292–11.364) |
| Non-total thyroidectomy    | 0.0614              | 0.6314                | 1.669 (0.246–13.514) |

Independent prognostic factors are highlighted in bold.

T, tumor size; N2, N ≥3 cm; LNEx, extranodal tumor extension; HR, Hazard ratio; CI, confidence interval
also demonstrated that patients with LNEx should be significant prognostic impact especially for patients aged die of thyroid carcinoma. This may be because recur-
to patient age. M1 and T4a2 were significant prognostic value of variables in high-risk patients according elucidate the reason for the difference in characteristics TNM classification, all patients with DTC aged <55 years are classified into Stage I, unless they have distant metastasis at diagnosis [1]. We also demonstrated that a cut off age of 55 years was a strong prognostic factor for CSS and overall survival of PTC patients [13]. In this study, CSS of intermediate-risk patients ≥55 years was similar to that of high-risk patients aged <55 years. Based on our results, high-risk patients <55 years old would be more appropriately re-categorized as intermediate-risk patients to more accurately reflect their prognoses. From this information, some uncertainty arises regarding how to implement patient-specific therapeutic strategies for high- and intermediate-risk patients according to age. For high-risk patients ≥55 years, there is no doubt that extensive therapies such as total thyroi-
dectomy, therapeutic/prophylactic lymph node dissec-
tions, adjuvant or therapeutic RAI administration and thyroid stimulating hormone (TSH) suppression are desirable if patients are otherwise healthy and have a good performance status. In our guidelines, for intermediate-risk patients, the extent of thyroidectomy and lymph node dissection should be implemented on a case-by-case basis by taking other prognostic factors, patient backgrounds, and patient choices into consideration. Since the prognosis of high-risk patients <55 years was similar to that of intermediate-risk patients ≥55 years, it may be assumed that therapeutic strategies of high-risk patients <55 years are the same as those of intermediate-risk patients. However, we also have to consider that younger patients have a much longer life expectancy than older patients; long-term preventative measures should be implemented for treating young patients to avoid carcinoma recurrence after the initial surgery. Verburg et al. demonstrated that life expectancy is significantly reduced only for patients ≥45 years with extensive local invasion, lateral lymph node metastases and/or distant metastasis [14]. However, they calculated a relative cumulative survival rate after 20 years at maximum and showed no data thereafter. Therefore, even though no distant metastasis is detected at the time of initial surgery, total thyroidectomy for young high-risk

| Variables        | Univariate analysis | Multivariate analysis | HR (95% CI) |
|------------------|---------------------|-----------------------|-------------|
| M1               | <0.0001             | <0.0001               | 14.493 (7.692–27.027) |
| T4a2             | <0.0001             | <0.0001               | 4.975 (2.538–9.709)  |
| T4a1             | 0.0177              | 0.0091                | 2.387 (1.241–4.587)  |
| T >4 cm          | 0.0159              | <0.0001               | 3.226 (1.926–5.405)  |
| N2               | 0.0005              | 0.0500                | 1.992 (1.000–3.968)  |
| LNEx             | 0.0161              | 0.2848                | 1.555 (0.693–3.497)  |
| Non-total thyroidectomy | 0.0534    | 0.1612                | 1.605 (0.828–3.115)  |

Independent prognostic factors are highlighted in bold.

T, tumor size; N2, N ≥3 cm; LNEx, extranodal tumor extension; HR, Hazard ratio; CI, confidence interval
patients might be still meaningful for monitoring postoperative thyroglobulin and in preparation for RAI therapy for distant recurrence, which may occur long afterwards. In contrast, unlike older high-risk patients, adjuvant RAI therapy or RAI ablation should not be strongly recommended immediately after surgery, unless thyroglobulin level is significantly elevated during postoperative follow-up. Similarly, young intermediate-risk patients showed favorable outcomes, but their CSS was still significantly poorer than that of very low- or low-risk patients. Therefore, it remains debatable whether intermediate-risk patients <55 years should be re-categorized to low-risk. In the guidelines, total thyroidectomy is not recommended for low- or very low-risk patients. Even though these patients are classified into low-risk, whether non-total thyroidectomy is adequate for a therapeutic strategy still remains unclear if we consider their long life expectancy.

There is also still some uncertainty regarding whether the age cutoff at 55 years is appropriate. Adams et al. demonstrated that patient age is associated with death-related carcinoma in a linear fashion [15]. They showed that ten-year CSS estimates showed a continuous decrease, 98.1% for 50–59 years, 94.8% for 60–69 years, 91.3% for 70–79 years, 79.2% for 80–89 years, and 73.9% for ≥90 years. However, this study was not a single institution study, but an analysis on patients from the SEER database (1998 to 2012), indicating that patients who underwent various kinds of therapy were enrolled. Chareau et al. published a single institution study demonstrating that very old patients (>75 years) showed a significantly poorer prognosis than younger patients, but they also showed that the incidence of high-risk patients was higher in very old patients [16]. We also investigated the prognosis of older patients in this series; however, we found that prognosis became poorer with age (60s, 70s, and 80s) for high-risk patients, but not for low- and intermediate-risk patients (data not shown). Therefore, only high-risk patients are candidates for future change in risk classification based on patient age.

Our study has some limitations. This is a retrospective study and the therapeutic strategies for PTC used during the study period were significantly different from those presently used. In our study, 22.5% of high-risk patients and 47.5% of intermediate-risk patients did not undergo total thyroidectomy. These incidences are definitely higher than present rates. Furthermore, prophylactic modified radical neck dissection was more frequently utilized during the study period compared to present practices. Moreover, a very limited number of patients (8.0% of high-risk patients, Table 1) underwent RAI ablation or adjuvant therapy (≥30 mCi). This is because, due to a limited capacity, many patients underwent RAI scintigraphy by administrating small amount of RAI (3–13 mCi), instead of RAI therapy or ablation using RAI ≥30 mCi. At present (since 2006), we changed our strategies and performed total thyroidectomies almost routinely for high-risk patients followed by RAI ablation or adjuvant RAI therapy, even though the patients were M0. Moreover, prophylactic modified radical neck dissection is now indicated only for PTC ≥3 cm and/or significant extrathyroid extension based on our previous study [17]. The difference in prognosis, including CSS, of high-risk patients before and after 2006 should be compared in future studies. Lastly, this risk classification does not include histology (i.e., to identify aggressive variants), molecular findings (such as BRAF and TERT mutations) or postoperative dynamic parameters such as thyroglobulin doubling-time and changes in anti-thyroglobulin antibody values [18, 19].

In summary, we demonstrated that the prognosis of high-risk patients <55 years was similar to that of intermediate-risk patients ≥55 years and therefore, we suggest that young high-risk patients can be re-classified as intermediate-risk in order to avoid overtreatment. The appropriate extent of thyroidectomy and lymph node dissection for young high-risk patients is still debatable; however, adjuvant RAI therapy or RAI ablation is not necessary unless thyroglobulin levels elevate during the follow-up. Young intermediate-risk patients have excellent prognoses, but since their prognoses are still poorer than low-risk patients, further studies should be done to elucidate whether these patients are regarded as low-risk.

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