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Impact of Additional Preoperative Computed Tomography Imaging on Staging, Surgery, and Postsurgical Survival in Patients With Papillary Thyroid Carcinoma

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Objective: We investigated the impacts of computed tomography (CT) added to ultrasound (US) for preoperative evaluation of patients with papillary thyroid carcinoma (PTC) on staging, surgical extent, and postsurgical survival.

Materials and Methods: Consecutive patients who underwent surgery for PTC between January 2015 and December 2015 were retrospectively identified. Of them, 584 had undergone preoperative additional thyroid CT imaging (CT + US group), and 859 had not (US group). Inverse probability of treatment weighting (IPTW) and propensity score matching (PSM) were used to adjust for 14 variables and balance the two groups. Changes in nodal staging and surgical extent caused by CT were recorded. The recurrence-free survival and distant metastasis-free survival after surgery were compared between the two groups.

Results: In the CT + US group, discordant nodal staging results between CT and US were observed in 94 of 584 patients (16.1%). Of them, CT accurately diagnosed nodal staging in 54 patients (57.4%), while the US provided incorrect nodal staging. Ten patients (1.7%) had a change in the extent of surgery based on CT findings. Postsurgical recurrence developed in 3.6% (31 of 859) of the CT + US group and 2.9% (17 of 584) of the US group during the median follow-up of 59 months. After adjustment using IPTW (580 vs. 861 patients), the CT + US group showed significantly higher recurrence-free survival rates than the US group (hazard ratio [HR], 0.52 [95% confidence interval {CI}, 0.29–0.96]; $P = 0.037$). PSM analysis (535 patients in each group) showed similar HR without statistical significance (HR, 0.60 [95% CI, 0.31–1.17]; $P = 0.134$). For distant metastasis-free survival, HRs after IPTW and PSM were 0.75 (95% CI, 0.17–3.36; $P = 0.71$) and 0.87 (95% CI, 0.20–3.80; $P = 0.851$), respectively.

Conclusion: The addition of CT imaging for preoperative evaluation changed nodal staging and surgical extent and might improve recurrence-free survival in patients with PTC.

Keywords: Thyroid; Thyroid cancer; Ultrasonography; CT; Recurrence

INTRODUCTION

Although papillary thyroid cancer (PTC) is associated with high overall survival rates exceeding 90%, PTC has a high rate of locoregional recurrence after operation [1]. Most recurrent thyroid cancer represents persistent disease due to

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incomplete preoperative staging or incomplete surgery [2-4]. Thus, most reoperations for recurrence are preventable with accurate initial preoperative workup.

Ultrasound (US) is the first-line imaging modality for patients with known or suspected thyroid cancer [5,6]. Current guidelines for differentiated thyroid cancers do not recommend the routine use of imaging beyond neck US before initial surgery, and preoperative computed tomography (CT) is recommended in case of clinical suspicion of advanced stages [5,6]. Recently, several studies have reported the added diagnostic value of CT imaging as an adjunct to US imaging in detecting lymph node (LN) metastasis from thyroid cancer [7-9]. In addition, preoperative CT imaging has a role in managing thyroid cancer patients by changing surgical planning, even in some low-risk patients with well-differentiated thyroid cancer [7,8,10,11].

Although several studies have investigated the diagnostic role of CT imaging in thyroid cancer patients, evidence regarding the survival benefit of performing preoperative CT imaging is lacking. Thus, in this study, we investigated the impacts of CT added to US for preoperative evaluation of PTC patients on staging, surgical extent, and postsurgical survival.

MATERIALS AND METHODS

Study Participants

The study population was obtained from a historical cohort of consecutive patients who underwent surgery for PTC at Asan Medical Center, a 2700-bed academic tertiary referral hospital, between January 2015 and December 2015. We excluded patients who had undergone thyroidectomy before (n = 21), were diagnosed with tumors other than PTC at histopathologic analysis (n = 43), undergone an operation for benign nodules (n = 32), or whose survival information was not available (n = 69).

The thyroid CT protocol was developed in November 2014 and was gradually incorporated into the preoperative evaluation of thyroid cancer. In Asan Medical Center, it is the general practice to first evaluate with US imaging for the initial diagnosis of thyroid cancer, and then the physicians and surgeons would additionally perform thyroid CT as their preference. During the study period, there was no change in the modality or method of management for PTC at our institution. Ultimately, we analyzed a series of 1443 patients (age range, 15–79 years; mean age, 47.5 years), which included 584 patients who had undergone preoperative thyroid CT imaging (CT + US group) and 859 had not (US group) (Fig. 1).

This retrospective study was approved by the Asan Medical Center institutional review board (IRB number 2019-1086). The requirement to obtain informed consent was waived.

US and CT Imaging Technique

US imaging was performed using an iU22 or HDI-5000 unit (Philips Healthcare), an EUB-7500 unit (Hitachi Medical Systems), or an S3000 unit (Siemens Healthineers) with a 5–14-MHz linear high-frequency probe. CT imaging was performed using a 128-channel CT scanner (Somatom Definition Flash; Siemens) with 80 and 140 kVp tube voltages. CT scanning began at the aorticopulmonary window and continued toward the skull base. CT was performed with the following parameters used consistently in all patients: 32 x 0.6 mm detector collimation, 0.5 s gantry rotation time, 1.0 pitch, 0.75 mm-thick sections, 0.7 mm-thick section increments, and a 256 x 256 matrix. An automated dose-reduction technique (CAREDose4D; Siemens) was used. For contrast enhancement, a 75 mL iodinated contrast agent (Omnipaque 300; GE Healthcare) was injected at a rate of 3.5 mL/s with a scan delay of 25 s. The contrast agent was administered into the right arm because of delayed contrast agent arrival due to compression of the left brachiocephalic vein, which is a potential problem if the left arm is used. Additionally, 50 mL of normal saline was injected at 3.5 mL/s immediately after administering the contrast agent to avoid artifacts caused by stagnated contrast agents within the subclavian or innominate vein [5]. A delayed scan was obtained 70 s after injection of the contrast media using the same scan parameters.

Image Analysis and Diagnostic Criteria

All CT and US images were interpreted as part of the routine clinical practice by radiologists under the supervision of staff radiologists with more than 14 years of clinical experience in head and neck radiology. Radiologists used the following predefined criteria of our institution, which have not changed since January 2014. LNs were interpreted as suspicious for metastasis if any one of the following features was present: calcification, cystic change, hyperechogenicity compared to the adjacent muscles, or peripheral or diffuse color Doppler pattern on US image and calcification, cystic change, focal or diffuse strong enhancement, or heterogeneous enhancement on CT.

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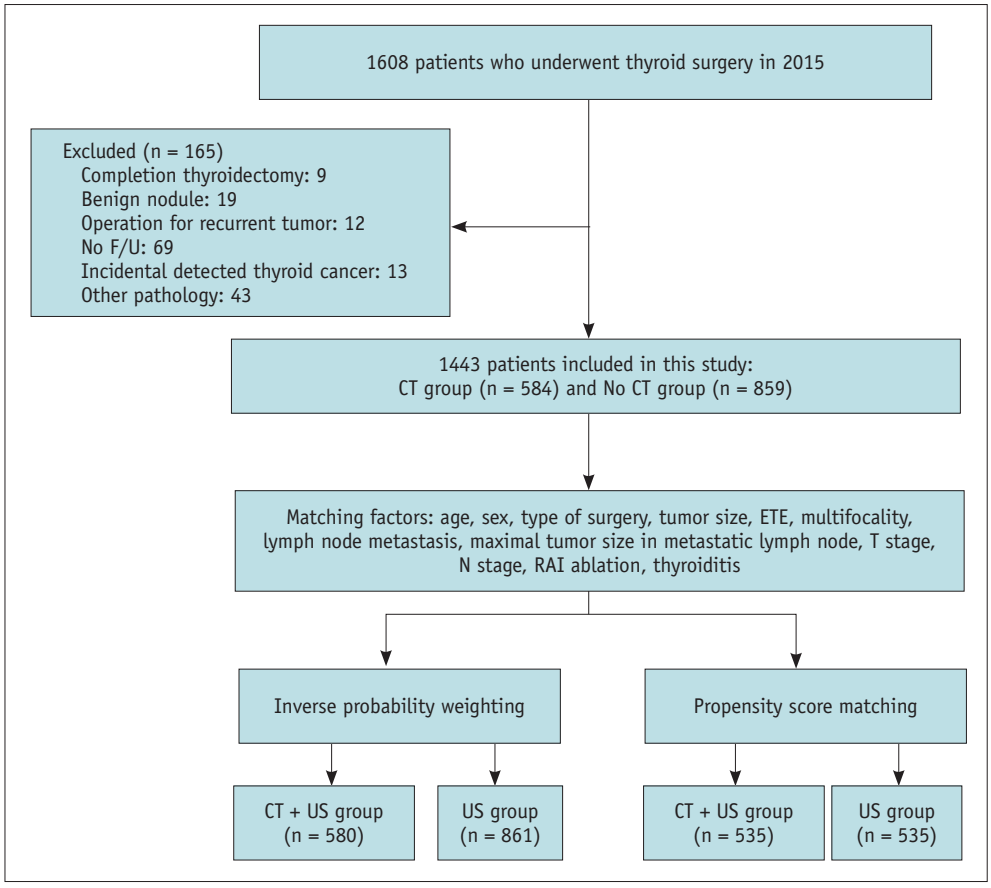

Fig. 1. Patient selection flow chart. F/U = follow-up, CT = computed tomography, ETE = extrathyroidal extension, RAI = radioactive iodine, US = ultrasound

Radiologists performed US-guided fine-needle aspiration (FNA) of suspicion for metastatic LNs when it affected the surgical extent of thyroid cancer, regardless of their size. Radiological benign or indeterminate LNs were examined at the clinician's request.

Follow-Up Protocol

Regardless of their surgical extent, all patients were regularly followed-up with physical examinations, thyroid function tests, serum thyroglobulin (Tg), and anti-Tg antibody measurements every 6–12 months for at least two years after surgery. Neck US was performed within the first 6–12 months after the initial surgery and was routinely repeated at 12- to 24-month intervals. If suspicious thyroid nodules or LNs were found, FNA was used for evaluation. Additional diagnostic imaging was performed to detect recurrence or distant metastasis in some patients, such as neck or chest CT, magnetic resonance imaging, or whole-body fluorodeoxyglucose positron emission tomography, as needed.

Outcomes

The primary outcomes were recurrence-free survival and distant metastasis-free survival. Recurrence of disease was defined by structural evidence of disease that was detected on various imaging studies since the initial surgery, which was confirmed by cytology or pathology. Distant metastasis was defined as the development of thyroid cancer foci at distant organs in areas other than the neck, which was either confirmed with a biopsy or clinically suspected based on various imaging studies.

The index date or zero-time was defined as the date the patient underwent surgery. Patients were followed up from this index date. Each patient's recurrence-free and distant metastasis-free survival times were computed from the index date to the last follow-up evaluation and confirmation of recurrence or distant metastasis. The routine follow-up protocol was identical in all patients and did not differ between the two groups.

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Statistical Analysis

All patients who met the eligibility criteria at baseline were included in the analyses. The characteristics of the two groups were compared using chi-square and a two-sampled T-test for categorical and continuous variables, respectively.

The propensity scores (PSs) were applied to cope with the potential imbalance of confounders between the two groups. The PSs of undergoing thyroid CT were estimated using a logistic regression model with the following baseline factors: age, sex, type of surgery, pathologic subtype of PTC, tumor size, presence of extrathyroidal extension, multifocality of tumor, metastatic LN in the central neck compartment or lateral neck compartment, maximal tumor size in the LN, T staging, N staging, radioactive iodine ablation and presence of thyroiditis. For propensity score matching (PSM), 1:1 Greedy nearest neighbor matching was performed without replacement within specified caliper widths. The standardized mean difference was used to check the balance in the observed covariates between the two groups. Variable balancing is considered to be achieved if the absolute standardized difference is < 0.1. Both inverse probability of treatment weighting (IPTW) and PSM were used for the analysis.

Kaplan–Meier curves were used to estimate recurrence-free survival and distant metastasis-free survival, and a Cox proportional hazards regression model was used to compare the survival between the two groups using hazard ratio (HR). An inverse probability-weighted Cox proportional hazards regression model was applied based on IPTW, and a Cox proportional hazards regression model with robust variance estimators to account for the clustering within matched sets on PSM. PSM was performed using SAS version 9.4 (SAS Institute, Inc.), and all other analyses were performed using R statistical software, version 3.6.3 (R Foundation for Statistical Computing).

RESULTS

Characteristics of the Study Population

Of 1443 patients, 584 (40.5%) had undergone preoperative thyroid CT imaging, and 859 (59.5%) had not. Eighty percent (1153 of 1443) of patients were diagnosed with the classic type of PTC, 13.5% (196 of 1443) of patients were diagnosed with a follicular variant of PTC, and 6.5% (94 of 1443) were diagnosed with the aggressive subtype of PTC. Aggressive subtypes of PTC included the tall cell variant (n = 75), columnar cell variant (n = 5), solid variant (n = 12), and diffuse sclerosing variant (n = 2). Regarding the tumor size, 858 patients (59.5%) underwent surgery for a tumor smaller than 1 cm.

Table 1 shows the baseline characteristics of patients in the study sample. Patients who underwent preoperative thyroid CT included a high proportion of women (81.8% vs. 74.5%; $P = 0.001$), patients who underwent total thyroidectomy (50.0% vs. 37.6%; $P < 0.001$), tumors larger than 1 cm (44.3% vs. 38.0%; $P = 0.013$), central neck LN metastasis (52.4% vs. 39.5%; $P < 0.001$), lateral neck LN metastasis (14.0% vs. 7.9%; $P < 0.001$), macro-metastasis in LN (37.3% vs. 27.7%; $P < 0.001$), pathologic T staging of III or IV (11.3% vs. 7.1%; $P = 0.006$), and pathologic LN metastasis (53.6% vs. 40.0%; $P < 0.001$).

After adjustment using PS analysis with IPTW, the standardized mean differences were all < 0.1, indicating a good covariate distribution balance between the groups (Table 1). For PS matching, 535 pairs of women were assigned to each group with well-balanced possible confounding variables, as in the IPTW.

Comparison of Nodal Staging Based on CT Imaging and US Imaging

In the CT + US group, discordant nodal staging results between CT and US were observed in 94 of 584 patients (16.1%). Of them, CT accurately diagnosed nodal staging in 54 patients (57.4%), while US provided incorrect nodal staging. On the other hand, CT had an incorrect diagnosis, but the US provided the correct nodal staging in 40 patients (42.6%). Among the 54 patients who had a correct nodal staging on CT, there were the following nodal staging comparisons between US and CT: N0 vs. N1a (US vs. CT) in 36 patients, N0 vs. N1b in 6 patients, N1a vs. N0 in 2 patients, N1a vs. N1b in 1 patient, N1b vs. N0 in 6 patients, and N1b vs. N1a in 3 patients (Table 2). Additional FNA was performed for ten patients diagnosed as N1b on CT imaging after N0 or N1a on US imaging.

Ten patients (1.7%) underwent a more extensive and accurate surgical intervention based on CT findings. Among them, seven initially had N0 or N1a staging in the US but were diagnosed with N1b staging on CT, leading to the performance of lateral neck dissection. Additionally, in 3 cases, CT confirmed LN metastasis in the retropharynx or level 7, which was not detected by the US, resulting in a broader surgical approach.

Recurrence-Free and Distant Metastasis-Free Survival

During the median follow-up of 59 months (range, 4–84

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Table 1. Baseline characteristics of patients

Variables	Unadjusted patients (n = 1443)		*P*	SMD	Inverse probability of treatment weighting analysis (n = 1441)		*P**	SMD	Propensity score–matched patients (n = 1070)		SMD
	US group (n = 859)	CT + US group (n = 584)			US group (n = 861)	CT + US group (n = 580)			US group (n = 535)	CT + US group (n = 535)	
Age											
< 55 yr	702 (81.7)	471 (80.7)	0.608	0.027	701 (81.4)	471 (81.2)	0.895	0.007	440 (82.2)	431 (80.6)	0.043
≥ 55 yr	157 (18.3)	113 (19.3)			160 (18.6)	109 (18.8)			95 (17.8)	104 (19.4)	
Sex											
Female	640 (74.5)	478 (81.8)	0.001	0.179	667 (77.5)	448 (77.3)	0.921	0.006	431 (80.6)	431 (80.6)	< 0.001
Male	219 (25.5)	106 (18.2)			194 (22.5)	132 (22.7)			104 (19.4)	104 (19.4)	
Type of surgery											
Less than total	536 (62.4)	292 (50.0)	< 0.001	0.252	494 (57.3)	335 (57.8)	0.902	0.007	298 (55.7)	290 (54.2)	0.030
Total	323 (37.6)	292 (50.0)			367 (42.7)	245 (42.2)			237 (44.3)	245 (45.8)	
Pathology PTC											
Classic	804 (93.6)	545 (93.3)	0.835	0.011	805 (93.5)	544 (93.8)	0.863	0.009	505 (94.4)	498 (93.1)	0.054
Aggressive	55 (6.4)	39 (6.7)			56 (6.5)	36 (6.2)			30 (5.6)	37 (6.9)	
Tumor size											
< 1 cm	533 (62.0)	325 (55.7)	0.013	0.157	512 (59.5)	347 (59.8)	0.981	0.011	313 (58.5)	307 (57.4)	0.030
1–2 cm	224 (26.1)	194 (33.2)			250 (29.0)	169 (29.1)			176 (32.9)	178 (33.3)	
> 2 cm	102 (11.9)	65 (11.1)			99 (11.5)	64 (11.1)			46 (8.6)	50 (9.3)	
ETE											
Absence	419 (48.8)	255 (43.7)	0.056	0.103	402 (46.7)	271 (46.7)	0.988	0.001	243 (45.4)	242 (45.2)	0.004
Presence	440 (51.2)	329 (56.3)			459 (53.3)	309 (53.3)			292 (54.6)	293 (54.8)	
Multifocality											
Absence	547 (63.7)	367 (62.8)	0.746	0.017	550 (63.9)	372 (64.1)	0.914	0.006	342 (63.9)	336 (62.8)	0.023
Presence	312 (36.3)	217 (37.2)			311 (36.1)	208 (35.9)			193 (36.1)	199 (37.2)	
Central LN positive											
Absence	520 (60.5)	278 (47.6)	< 0.001	0.262	475 (55.2)	319 (55.0)	0.982	0.001	278 (52.0)	272 (50.8)	0.022
Presence	339 (39.5)	306 (52.4)			386 (44.8)	261 (45.0)			257 (48.0)	263 (49.2)	
Lateral LN positive											
Absence	791 (92.1)	502 (86.0)	< 0.001	0.197	773 (89.8)	521 (89.8)	0.970	0.002	480 (89.7)	474 (88.6)	0.036
Presence	68 (7.9)	82 (14.0)			88 (10.2)	59 (10.2)			55 (10.3)	61 (11.4)	
Max. LN tumor size											
No dissection or missing	517 (60.2)	274 (46.9)	< 0.001	0.269	470 (54.6)	316 (54.5)	0.998	0.004	275 (51.4)	270 (50.5)	0.028
< 2 mm	104 (12.1)	92 (15.8)			117 (13.6)	80 (13.8)			78 (14.6)	76 (14.2)	
≥ 2 mm	238 (27.7)	218 (37.3)			274 (31.8)	184 (31.7)			182 (34.0)	189 (35.3)	
T stage											
1 or 2	798 (92.9)	518 (88.7)	0.006	0.146	783 (90.9)	530 (91.4)	0.753	0.018	492 (92.0)	486 (90.8)	0.040
3 or 4	61 (7.1)	66 (11.3)			78 (9.1)	50 (8.6)			43 (8.0)	49 (9.2)	
N stage											
0	515 (60.0)	271 (46.4)	< 0.001	0.274	468 (54.4)	314 (54.1)	0.972	0.002	273 (51.0)	267 (49.9)	0.022
1	344 (40.0)	313 (53.6)			393 (45.6)	266 (45.9)			262 (49.0)	268 (50.1)	
RAI treatment											
Treated	619 (72.1)	336 (57.5)	< 0.001	0.308	569 (66.1)	382 (65.9)	0.950	0.003	338 (63.2)	334 (62.4)	0.015
Not treated	240 (27.9)	248 (42.5)			292 (33.9)	198 (34.1)			197 (36.8)	201 (37.6)	
Thyroiditis											
Absence	595 (69.3)	406 (69.5)	0.918	0.006	599 (69.6)	403 (69.5)	0.944	0.004	374 (69.9)	372 (69.5)	0.008
Presence	264 (30.7)	178 (30.5)			262 (30.4)	177 (30.5)			161 (30.1)	163 (30.5)	

Data are presented as n (%) unless otherwise indicated. Counts in the weighted cohort may not sum to expected totals owing to rounding. Percentages may not total 100 because of rounding, and disagreements between numbers and percentages in the weighted cohort are the result of rounding of noninteger number values.

*For categorical variables, chi-square test was used, and n (%) was reported.

US = ultrasound, CT = computed tomography, SMD = standardized mean difference, PTC = papillary thyroid carcinoma, ETE = extrathyroidal extension, LN = lymph node, Max. = maximum, RAI = radioactive iodine

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Table 2. Comparison of discordant nodal staging results in PTC patients between CT imaging and US imaging

US nodal staging	Total	CT nodal staging					
		N0		N1a		N1b	
		Correct	Incorrect	Correct	Incorrect	Correct	Incorrect
N0	472	N/A		36	20	6	9
N1a	25	2	8	N/A		1	1
N1b	87	6	1	3	1	N/A	

Data are number of patients. "Correct" indicates accurate nodal staging on CT imaging but inaccurate nodal staging on US imaging, while "incorrect" denotes inaccurate nodal staging on CT imaging but accurate nodal staging on US imaging.
PTC = papillary thyroid carcinoma, CT = computed tomography, US = ultrasound, N/A = not available

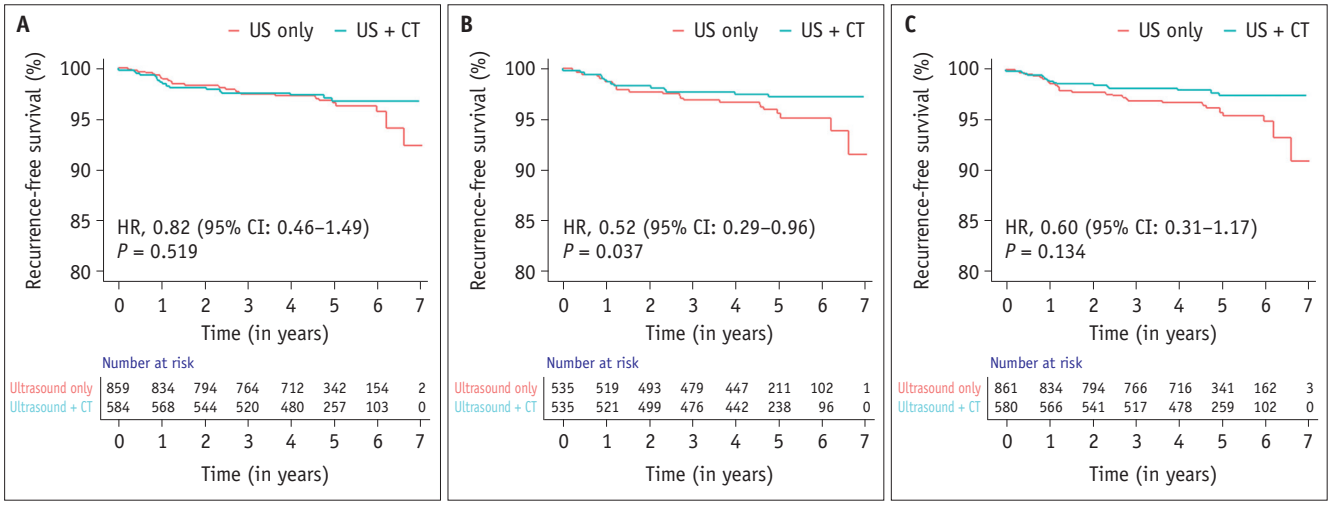

Fig. 2. Kaplan-Meier plots of recurrence-free survival of CT + US group and US-only group in the unadjusted **(A)**, IPTW **(B)**, and propensity score matched **(C)** samples. CT = computer tomography, US = ultrasound, IPTW = inverse probability of treatment weighting, HR = hazard ratio, CI = confidence interval

months), 3.6% (31 of 859) of patients in the CT + US group and 2.9% (17 of 584) in patients in the US group developed recurrence. Before matching, there was no significant difference in recurrence-free survival according to the Kaplan-Meier analysis between the CT + US group and US imaging group (P = 0.519) (Fig. 2). However, after adjustment using IPTW, the CT + US group showed significantly higher recurrence-free survival rates than the US imaging with an HR of 0.52 (95% confidence interval [CI], 0.29–0.96; P = 0.037). The estimated 7-year recurrence-free survival rates were 97.5% in the CT imaging group and 90.9% in the non-CT imaging group. Using PSM, HR for recurrence-free survival was 0.60 without statistical significance (95% CI: 0.31–1.17; P = 0.134) (Fig. 2, Table 3). For distant metastasis-free survival, the HRs after IPTW and PSM were 0.75 (95% CI: 0.17–3.36; P = 0.71) and 0.87 (95% CI: 0.20–3.80; P = 0.851), respectively (Table 3).

DISCUSSION

In this study, we assessed whether additional CT imaging evaluation improved the clinical outcomes of patients diagnosed with PTC. Our observational study showed that adding CT imaging as a preoperative evaluation changed nodal staging and surgical extent and might improve recurrence-free survival in patients with PTC. A significantly higher recurrence-free survival of patients in the CT + US group than in the US group was observed in the IPTW analysis. To our knowledge, this is the first study to evaluate the effect of preoperative CT imaging on clinical outcomes using IPTW and PSM methods to adjust for potential confounding factors and to create a balance between the two groups.

PTCs are associated with good prognoses and a low mortality rate. However, the high recurrence rate remains a major concern, and it has been reported to be as high as 35% [1,4]. However, most patients required reoperation for recurrent tumors diagnosed within 24 months after their

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Table 3. Unadjusted and adjusted hazard ratios of clinical outcomes

Outcome	Model	Hazard ratio (95% CI)	*P*
Recurrence free survival	Unadjusted	0.82 (0.46–1.49)	0.519
(CT + US group vs. US group [control])	IPTW	0.52 (0.29–0.96)	0.037
	PSM	0.60 (0.31–1.17)	0.134
Distant metastasis	Unadjusted	1.25 (0.28–5.70)	0.772
(CT + US group vs. US group [control])	IPTW	0.75 (0.17–3.36)	0.710
	PSM	0.87 (0.20–3.80)	0.851

Unadjusted model include 584 and 859 patients for CT + US and US groups, respectively, IPTW model include 580 and 861 patients, respectively, and propensity score matched model include 535 patients for each group.
CT = computed tomography, US = ultrasound, IPTW = inverse probability of treatment weighting, CI = confidence interval, PSM = propensity score matched

initial operation [2-4]. It is accepted that most of the recurrent disease following initial curative therapy for PTC represents persistent disease due to incomplete preoperative staging or incomplete surgery [2,4,12]. Therefore, the importance of accurate nodal staging and evaluation of its location in preoperative evaluation is emerging.

Several studies have addressed the diagnostic value of US and CT for the preoperative diagnosis of node metastasis from PTC [8,9,13,14]. When the diagnostic performance of combined CT and the US is compared with that of the US alone, the diagnostic sensitivity for diagnosing LN metastasis is improved significantly in the lateral neck compartment [7,8,13,15,16]. In our study, correct CT imaging diagnoses in nodal staging of PTC were noted in 54 patients and changes in surgical extent in 10 patients (1.7%). Previous findings about preoperative CT for surgical planning in PTC patients are consistent with our data [7,10]. Lesnik et al. [7] found that adding CT to the preoperative workup of patients with newly diagnosed PTC changed the surgical plan in 25% of patients. Bongers et al. [10] also found that adding CT changed the surgical plan of 22.5% of patients with clinically low-risk PTC. However, compared to the previous two studies, the percentage of change in surgical plan was low in our study. In our study, we performed preoperative additional FNA for additionally detected pathologic LNs on CT, whereas the other two studies performed surgery without preoperative confirmation.

These changes in the nodal staging and surgical extent may influence improved recurrence-free survival in the CT + US group. To obtain an accurate analysis of the effect of CT imaging on clinical outcomes, balanced groups are necessary because the unadjusted patients in our study had heterogeneous features. In the IPTW analysis, the recurrence-free survival of the CT + US group was significantly higher than in the US group. In PSM analysis, although the *P*-value did not indicate a statistically significant difference at a level of 0.05, we observed a consistent trend with the IPTW results, as evidenced by a HR of 0.6. The lack of statistically significant differences in the PSM analysis may be attributed to the limited sample size and the selective nature of the population. Thus, further studies with a larger number of patients may be needed to validate these findings. In addition, regarding distant metastasis-free survival, there was no significant difference observed between the CT + US group and the US group. This lack of significance may be attributed to the small sample size of patients (n = 7) who experienced metastasis.

Although we showed the clinical benefits of CT imaging in addition to US imaging evaluation for patients with PTC, additional imaging may have also had adverse effects, including overdiagnosis. In our study, 42.6% of patients who showed changed nodal staging after CT imaging had changes proven inappropriate, with the majority being attributed to false positive staging of N1a or N1b of CT among initially N0 staging on US. These included ten patients who received unnecessary FNA due to false positive LN located in the lateral neck compartment on CT. However, when considering the fact that FNA is a minimally invasive procedure compared to repeated surgery for persistent metastatic LNs, the clinical benefits of accurate nodal staging provided by CT may outweigh the risks of unnecessary FNA due to false positive results from CT. All cases of false positive results on CT were due to arterial hyperenhancement within the LN. The criteria for judging the hyperenhancement of LN on CT have not yet been clearly established. The degree of enhancement of LN is affected not only by metastatic foci with accompanying hypervascularity, but also by the body weight of the patients, scan time, and amount of injected contrast agent [17]. Therefore, to reduce overdiagnosis and subsequent unnecessary FNA of LNs, an objective cutoff for

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the hyperenhancement of LN on CT is needed.

The major limitation of this study was that it was based on observational data, and there was a possibility of unavoidable selection bias. To minimize the selection bias, we used multiple strategies, including using a large number of patients, intention-to-treat analyses, an extensive comparison of patients' baseline characteristics, and adjustment for confounders by using inverse probability weighting and PSM. However, there may be unobserved characteristics that may be associated with clinical outcomes [18]. Second, the patient data of this study were obtained from a single tertiary referral center. CT images taken were of high quality using thyroid-specific protocols [19], and experienced radiologists performed image analysis. Therefore, our results may not be reproducible in community hospitals with less expertise. Third, the long-term survival outcomes of patients were not evaluated.

In conclusion, our present cohort study showed that adding CT imaging as a preoperative evaluation changed nodal staging and surgical extent and might improve recurrence-free survival in PTC patients.

Availability of Data and Material

The datasets generated or analyzed during the study are not publicly available due to privacy protection and ethics division principle but are available from the corresponding author on reasonable request.

Conflicts of Interest

Jeong Hyun Lee, the section editor, and Jung Hwan Baek, the editor board member of the *Korean Journal of Radiology*, were not involved in the editorial evaluation or decision to publish this article. All authors have declared no conflicts of interest.

Author Contributions

Conceptualization: Sae Rom Chung. Data curation: So Yeong Jeong, Sae Rom Chung, Jung Hwan Baek, Young Jun Choi, Tae-Yon Sung, Dong Eun Song, Tae Yong Kim, Jeong Hyun Lee. Formal analysis: So Yeong Jeong, Sae Rom Chung. Methodology: So Yeong Jeong, Sehee Kim. Project administration: Sae Rom Chung. Resources: So Yeong Jeong, Sae Rom Chung. Software: Sae Rom Chung, Sehee Kim. Supervision: Sae Rom Chung, Jeong Hyun Lee. Validation: Sae Rom Chung. Visualization: Sae Rom Chung, Sehee Kim. Writing—original draft: So Yeong Jeong. Writing—review & editing: all authors.

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