

Shear-wave elastography in thyroid ultrasound

Can be a predictor of extrathyroidal extension and cervical lymph node metastasis in papillary thyroid carcinoma?

Dong Yoon Han, MD, PhD^a, Yu-Mee Sohn, MD, PhD^{a,*}, Mirinae Seo, MD, PhD^a, Seong Jong Yun, MD, PhD^b, Won Seo Park, MD, PhD^c, Seok Ho Jeon, MD^d, Yong Hyun Cho, MD^d

Abstract

This study aimed to investigate whether extrathyroidal extension (ETE) and cervical lymph node metastasis (LNM) can be predicted using elasticity parameters of shear-wave elastography (SWE) combined with B-mode ultrasound (US) of papillary thyroid carcinomas (PTCs).

We retrospectively reviewed 111 patients who underwent preoperative SWE evaluation among PTC patients from July 1, 2016 to June 20, 2018. Patients were divided into 2 groups based on the presence or absence of ETE based on pathology reports. Univariate and multivariate analyses of clinical and radiologic features including B-mode US features, US patterns, and SWE parameters were performed. These analyses were repeated in LNM positive and negative groups. The diagnostic performance of SWE parameters were also evaluated.

Of the 111 patients, 33 had ETE, 78 did not have ETE, 44 had LNM, and 67 did not have LNM. A taller-than-wide shape and T3 stage on US were associated with ETE. Female sex, total thyroidectomy, and T3 stage on US were associated with LNM. When B-mode US and SWE were combined, there was no improvement in diagnostic performance.

Combination of SWE and B-mode US findings is not useful for predicting ETE and LNM status in PTC patients.

Abbreviations: ATA = American Thyroid Association, CIs = confidence intervals, EMRs = electronic medical records, ETE = extrathyroidal extension, FNAB = fine-needle aspiration biopsy, FTC = follicular thyroid cancer, LNM = lymph node metastasis, ORs = odds ratios, PTC = papillary thyroid cancer, ROC = receiver operating characteristic, ROI = region-of-interest, SWE = shear-wave elastography, US-FNAB = ultrasound-guided fine needle aspiration.

Keywords: B-mode ultrasonography, extrathyroidal extension, lymph node metastasis, papillary thyroid carcinoma, shear-wave elastography

1. Introduction

In Korea, thyroid cancer is the second most common cancer in women and the sixth most common in men.^[1] Thyroid cancer is

divided into several types, of which papillary thyroid cancer (PTC, 84%) and follicular thyroid cancer (FTC, 11%) account for more than 95% of cases.^[2] The prognosis of PTC is known to be relatively favorable with a mortality rate of less than 10%.^[3] However, there are several factors that indicate a poor prognosis; presence of extrathyroidal extension (ETE), tumor size greater than 1 or 2 cm, age 45 years old or older, multifocality, regional lymph node metastasis (LNM), familial history of thyroid cancer, and distant metastasis.^[4] If any of these factors are present, total thyroidectomy is performed rather than lobectomy.^[4] However, evaluation of prognostic factors before surgery is important because total thyroidectomy is associated with complications such as recurrent laryngeal nerve damage and hypoparathyroidism.^[5] Because accurate evaluation of ETE is important, many researchers have investigated factors that can predict ETE, but no factor identified to date has sufficient sensitivity and specificity.

ETE was first described by Woolner et al^[6] in 1961; these authors documented how among patients diagnosed with PTC, those with locally and highly infiltrative tumors had a poor prognosis. Since then, much research has been done on ETE, and many studies have evaluated the ability of US or CT findings to predict ETE. Kwak et al^[7] reported that ETE can be predicted relatively accurately if more than 25% of the tumor is in contact with the capsule. Previous studies on ETE have mostly used morphological approaches with ultrasound. However, to our knowledge, none of the previous studies have evaluated the ability of elasticity parameters of shear-

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

^aDepartment of Radiology, Kyung Hee University Hospital, College of Medicine, Kyung Hee University, Seoul, ^bDepartment of Radiology, G SAM Hospital, 591 Gunpo-ro, Gunpo-si, Gyeonggi-do, ^cDepartment of Surgery, Kyung Hee University Hospital, College of Medicine, Kyung Hee University, ^dDepartment of Anesthesiology and Pain Medicine, Seoul Sacred Heart General Hospital, 259 Wangsan-ro, Dongdaemun-gu, Seoul, South Korea.

*Correspondence: Yu-Mee Sohn, Department of Radiology, Kyung Hee University Hospital, College of Medicine, Kyung Hee University, 23 Kyungheedaero, Dongdaemun-gu, Seoul 02447, South Korea (e-mail: sonyume@naver.com).

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wave elastography (SWE) to predict ETE in patients with thyroid cancer.

Elastography is divided into strain elastography and SWE. Strain elastography is a relatively common method used in breast cancer to measure the degree of distortion of tissue by applying an external force or a mechanical force created by an ultrasound beam.^[8,9] Use of strain elastography to evaluate thyroid lesions is still controversial, as measurements can differ depending on the examiner and quantification is difficult.^[10,11] SWE is a method that uses mechanical vibration and quantitative elastography.^[12] Induced displacement at the focus creates a shear wave that provides information about the local viscoelastic properties of the tissue, thus allowing quantitation of elastic values.^[12] This new technique is less dependent on the examiners than strain elastography, and has also demonstrated higher diagnostic performance in differentiating thyroid nodules.^[13] However, the majority of studies have used SWE to distinguish between malignant and benign thyroid nodules; no study has used SWE to distinguish between the presence or absence of ETE as a risk factor for thyroid cancer. Therefore, we investigated whether SWE parameters could predict ETE in patients with thyroid cancer, and whether cervical LNM, another risk factor for thyroid cancer, could be predicted.

2. Methods

2.1. Patients

Our retrospective study was approved by the institutional review board of our institute before starting the study and the requirement for informed consent was waived. We identified 152 thyroid nodules in 140 consecutive patients who underwent thyroid ultrasound and SWE before ultrasound-guided fine needle aspiration (US-FNAB) between July 1, 2016 and June 20, 2018. Of these 152 nodules, 41 lesions in 29 patients were excluded for the following reasons:

1. lack of surgical confirmation (18 lesions in 16 patients),
2. at least 1 of the 4 SWE parameters (E_{max}, E_{mean}, E_{min}, E_{ratio}) missing (9 lesions excluded, in 8 patients who are still included in study cohort) or measured in different units (9 lesions in 8 patients), or
3. pathological diagnosis other than PTC, for example medullary thyroid carcinoma or a benign lesion (5 lesions in 5 patients).

Finally, 111 lesions of 111 patients were included. All these lesions were confirmed to be PTC. The reference standards for the presence or absence of ETE and LNM were the pathological results. Patients comprised 30 males and 81 females. The average age of the patients was 48.9 ± 11.9 years (range, 22–79 years).

2.2. B-mode US examinations, US features, and US-FNAB

Two radiologists with 11 and 7 years of ultrasound experience, respectively (Y-M. S. and M. S.) performed US examinations. B-mode US and SWE images were obtained sequentially for all US examinations by the same radiologists. B-mode US was performed with a high-resolution sonographic unit using 5 to 12 MHz and 4 to 15 MHz linear-array transducers (ATL HDI 5000, Philips Healthcare-Advanced Technology Laboratories, Bothell WA, USA; iU22, Philips Healthcare-Advanced Technology Laboratories, Bothell WA, USA; Aixplorer, SuperSonic Imagine, Aix en Provence, France). The patients position was supine with neck hyperextension. The following characteristics of

thyroid lesions according to B-mode US findings were recorded: composition (solid, mixed), echogenicity (marked hypoechoic, hypoechoic, isoechoic), microcalcification (presence, absence), margin (circumscribed, irregular), and shape (wide than taller, taller than wider). Thyroid nodules were not mixed echoic because our patient group comprised only those patients with thyroid cancer. Therefore, echogenicity was divided into 3 types: marked hypoechoic, hypoechoic, and isoechoic. Using the US features of these 5 categories, nodules were divided into 3 sonographic patterns as follows: high suspicion, intermediate suspicion, and low suspicion. This was based on the 2015 American Thyroid Association (ATA) management guidelines for adult patients with thyroid nodules.^[14] The 2015 ATA guidelines divide sonographic pattern into 5 categories: high (risk of malignancy, >70%–90%), intermediate (10%–20%), low (5%–10%), very low suspicion (<3%), and benign (<1%).^[14] US features of high suspicion are solid hypoechoic or a solid hypoechoic portion of a partially cystic nodule with 1 or more of the following features: microcalcifications, irregular margins, a small extrusive solid component with rim calcifications, taller-than-wide shape, and evidence of ETE. US features of intermediate suspicion are smooth margins with a hypoechoic solid nodule without ETE, microcalcifications, and taller-than-wide shape.^[14] US features of low suspicion are hyperechoic solid nodules or eccentric solid areas with a partially cystic nodule, isoechoic lesions, those without an irregular margin, microcalcifications, taller-than-wide shape, or ETE.^[14] There were no sonographic patterns corresponding to very low suspicion and benign because all of our study patients were operated on. ETE of a nodule was recognized when there was invasion of 1 or more of the strap muscles such as the sternohyoid, sternothyroid, thyrohyoid, or omohyoid muscles.^[15] US findings of LNM were defined as cystic changes, loss of fatty hilum, round shape, hyperechogenicity, and calcification.^[16] Based on the AJCC 8th edition guidelines, lesions were classified as N1a when central neck LNM was suspected and N1b when lateral neck LNM was suspected. In addition, nodule size (longest diameter) was also described as more than 1 cm or less than 1 cm.

A fourth-grade radiologic resident (D.Y.H.) performed imaging interpretation of the ultrasound images. Findings were made by consensus through discussion with a radiologist (Y-M.S.) with 11 years of experience. We classified thyroid nodules according to the 2015 ATA guidelines as high suspicion, intermediate suspicion, or low suspicion lesions based on US features.^[14] Because fine-needle aspiration biopsy (FNAB) is recommended for all of these categories of lesions, all patients underwent FNAB. US-FNAB was performed for solid portions of all suspicious nodules at least twice using a 23-gauge needle and a 2-ml syringe. Local anesthesia was not performed routinely. Aspirated material was ejected onto at least 2 slides and slides were soaked immediately in 95% ethanol solution. Slides were then transferred to cytopathologists for analysis. US-FNAB for 42 lesions was performed outside our institution, while US-FNAB for 71 lesions was performed at our institution. US-FNAB performed in our hospital was performed by the same 2 radiologists (Y-M.S. and M.S.) who used conventional US, and all nodules were found to be PTC.

2.3. SWE examination

After B-mode US, SWE scans of suspicious malignant nodules were performed using a 4 to 15 MHz linear-array transducer

(Aixplorer, SuperSonic Imagine, Aix en Provence, France). The patient’s position was the same as that described for B-mode US, and the operator took care not to compress the patients neck with the probe to minimize the probes impact on elasticity parameters. The color map obtained by SWE scans was overlaid on the B-mode US and comprised a continuous color spectrum with the lowest stiffness indicated in blue and the highest in red (0–180 kPa). After optimal SWE images were obtained, one 2-mm diameter circular region-of-interest (ROI; Q-box; Super Sonic Imagine) was placed where the thyroid nodule showed the highest stiffness, while the second ROI was placed on the normal thyroid parenchyma. The SWE system automatically calculated elasticity parameters. Emax is the maximum value of the ROI, Emean is the mean value of the ROI, Emin is the minimum value of the ROI, and Eratio is the ratio of the mean stiffness of the thyroid nodule to that of the normal thyroid parenchyma.

2.4. Histopathological evaluation

Patient electronic medical records (EMRs) were reviewed and patients were divided into total thyroidectomy and subtotal or lobectomy groups. Histopathologic reports were analyzed to determine the presence of ETE, presence of LNM, T stage, and N stage.

2.5. Statistical analysis

The independent t-test or Mann–Whitney *U* test was performed to compare continuous variables between groups, while Pearson Chi-Squared test or Fisher exact test was performed to compare nominal variables between groups. Multivariate logistic regression analysis was applied to determine independent predictive factors for ETE and LNM of thyroid cancer. Multivariate logistic regression analysis was conducted on those variables that were found to be statistically significant in univariate analysis. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were generated from the multivariate analyses.

To determine predictive performance and the cut-off values of B-mode US and elasticity parameters for ETE, receiver operating characteristic (ROC) curve analyses were performed and areas under the ROC curves (AUCs) were calculated. Diagnostic accuracies, sensitivities, and specificities were calculated for B-mode US alone, SWE alone, and the combination of B-mode US and SWE using the cut-off values of B-mode US and elasticity parameters. All statistical analyses were performed using MedCalc software (Version 12.3.0, Mariakerke, Belgium). *P* values <.05 were considered statistically significant.

3. Results

3.1. Demographics and sonographic and clinical characteristics of nodules with ETE

Of 111 nodules diagnosed as PTC, 33 were ETE positive and 78 were ETE negative. There were 12 men and 21 women in the ETE positive group, with an average age of 52.5 ± 14.0 years and a range of 27 to 81 years. The ETE negative group had 18 men and 60 women, with an average age of 47.3 ± 11.0 years and a range of 22 to 75 years (Table 1).

ETE positive group was older than the ETE negative group (*P* = .037). Total thyroidectomy was performed more frequently than subtotal thyroidectomy in the ETE positive group (*P* = .049). Nodule size measured by US was larger in the ETE positive group

Table 1
Comparison of US features, SWE parameters, and clinicopathologic factors for predicting ETE.

Variable	ETE (+) (n=33)	ETE (-) (n=78)	<i>P</i> value
Age	52.5 ± 14.0	47.3 ± 11.0	.037
Sex			.17
Male	12	18	
Female	21	60	
Surgery			.049
Subtotal thyroidectomy or lobectomy	21	64	
Total thyroidectomy	12	14	
Size (group)			.036
<10 mm	13	49	
≥10 mm	20	29	
Composition			1.0
Solid	32	75	
Mixed	1	3	
Echogenicity			.43
Iso	4	4	
Hypo	22	58	
Marked hypo	7	16	
Margin			.34
Circumscribed	6	22	
Irregular	27	56	
Microcalcification			.68
No	12	32	
Yes	21	46	
Shape			.051
Wider than tall	7	33	
Taller than wide	26	45	
ATA US pattern			1.0
Low	0	2	
Indeterminate	4	9	
High	29	67	
T stage on US			<.001
T1 (absence of ETE)	10	62	
T3 (presence of ETE)	23	16	
N stage on US			.29
NO	25	66	
N1a/1b	8	12	
Emax (kPa)	59.5 ± 44.3	66.1 ± 41.8	.49
Emean (kPa)	45.7 ± 34.0	50.5 ± 30.3	.49
Emin (kPa)	27.1 ± 23.6	32.1 ± 22.2	.29
Eratio	4.6 ± 3.7	5.1 ± 6.1	.60

Emax = maximum value for a fixed 2-mm diameter circular ROI placed in the stiffest area, Emean = mean value for the ROI, Emin = minimum value for the ROI. Continuous variables are expressed as means ± standard deviations.

(13.5 ± 9.0 mm) than in the negative group (9.8 ± 5.7 mm) (*P* = .036). The 4 elasticity parameters (Emin, Emean, Emax, Eratio) measured by SWE scan were not significantly different between the ETE positive and negative groups (Figs. 1 and 2). Among the 5 sonographic findings suggestive of malignant nodules, a taller-than-wide shape was borderline significantly higher in the ETE positive group than the ETE negative group (*P* = .051). More tumors were stage T3 according to US in the ETE positive group than in the ETE negative group (*P* < .001) (Table 1).

3.2. Factors predictive of ETE

On multivariate logistic regression analysis, T3 staging on US (OR = 6.0, *P* = .001) and taller-than-wide shape (OR = 3.4, *P* = .035) were independent predictors of ETE (Table 2).

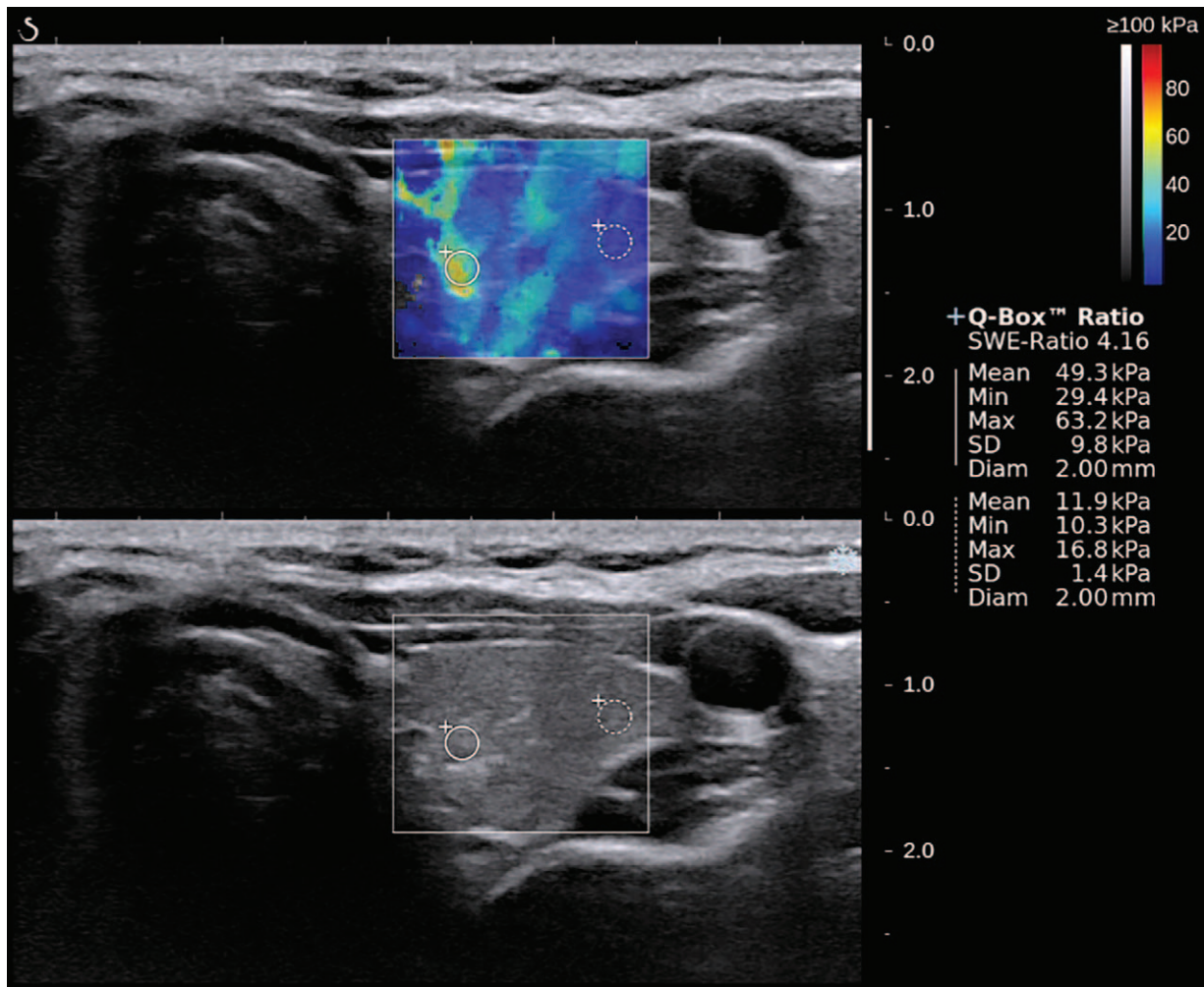


Figure 1. A 28-year-old female patient with PTC in the left thyroid gland was confirmed to have no ETE through surgery. The size of the mass was 7 mm, the B-mode US indicated the absence of ETE, and all 4 elasticity parameters of SWE were higher than the cut-off values. SWE findings were true negative results.

3.3. Demographics, sonographic, and clinical characteristics of patients with LNM

Of the 111 PTC patients, 44 had LNM while 67 had no LNM. There were 18 men and 26 women in the LNM group, with an average age of 48.1 ± 15.1 years and a range of 22 to 81 years. The no LNM group comprised 12 men and 55 women with an average age of 49.4 ± 9.8 years and a range of 25 to 75 years (Table 3).

LNM was more frequently found in female than male patients (59.1% vs 41.9%, respectively, $P = .009$). In patients with LNM, total thyroidectomy was performed more often than subtotal thyroidectomy ($P = .003$). Furthermore, the larger the thyroid nodule, the more LNM occurred ($P = .012$). LNM was more common in the group with ETE on US (T3 stage on US) ($P = .003$). Elasticity parameters of the thyroid nodule were not associated with LNM (Table 3). E ratio was slightly higher in the LNM positive group than the LNM negative group, but this difference was not statistically significant.

3.4. Factors predictive of LNM

On multivariate logistic regression analysis, female sex (OR = 3.0, $P = .012$), T3 staging on US (OR = 3.0, $P = .027$), and total

thyroidectomy (OR = 3.3, $P = .020$) were independent predictors of LNM (Table 4).

3.5. Diagnostic performance of US T-staging and elasticity parameters with optimal cut-off values and combination US T-staging and elasticity parameters for predicting ETE

Diagnostic performance of all elasticity parameters for prediction of ETE were significantly lower than those of B-mode US parameters based on AUC analyses. The optimal cut-off values of elasticity parameters to predict ETE were as follows: Emax 43.2 kPa; Emean 30.3 kPa; Emin 13.1 kPa; Eratio 2.0.

When the elasticity parameters of B-mode US and SWE were combined, specificities were higher (combined Emax: 84.6%, combined Emean: 83.3%, combined Emin: 82.1%, combined Eratio: 80.8%) than that of B-mode US alone (79.5%) but without statistical significance. In addition, sensitivity, PPV, NPV, and accuracy of combined B-mode US and SWE were all lower than the corresponding values for B-mode US (Tables 5 and 6).

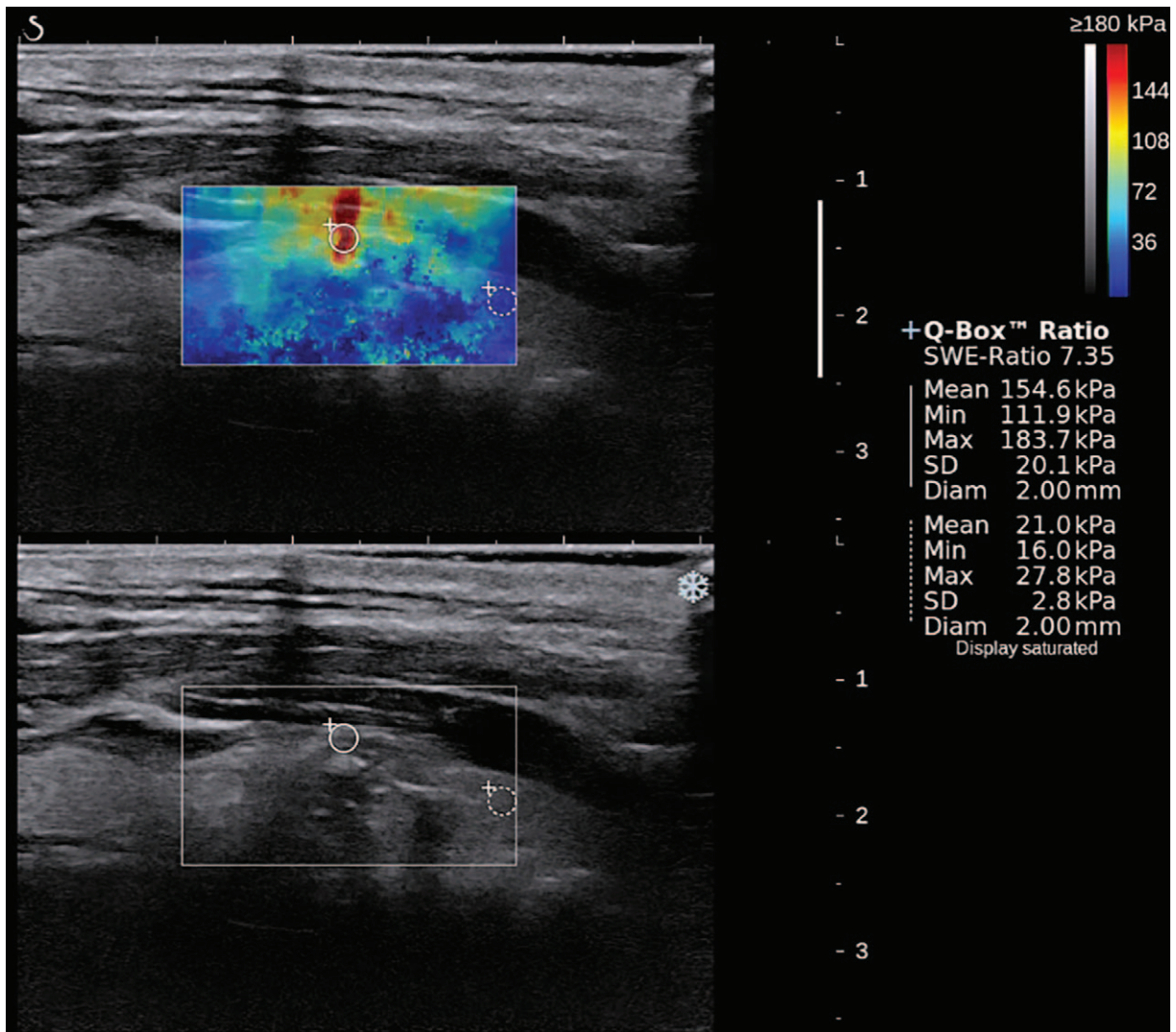


Figure 2. A 54-year-old man with PTC in the right thyroid gland was confirmed to have ETE through surgery. Mass was 13mm, and B-mode US indicated the presence of ETE, but all 4 elasticity parameters of SWE were higher than the cut-off value. SWE findings were false negative findings.

Table 2
Identification of independent clinical and radiological factors predictive of ETE using multiple regression analysis.

Variable	OR	95% CI	P value
Age	1.0	0.98, 1.1	.34
Size	1.8	0.60, 5.2	.30
Surgery			.89
Subtotal thyroidectomy or lobectomy	Ref.		
Total thyroidectomy	1.1	0.33, 3.6	
Shape			.035
Wider than tall	Ref.		
Taller than wide	3.4	1.1, 10.3	
T stage on US			.001
T1 (absence of ETE)	Ref.		
T3 (presence of ETE)	6.0	2.0, 17.7	

95% CI = 95% confidence interval, OR = odds ratio, Ref. = reference.

4. Discussion

ETE and the presence of metastatic LNs are known to increase the risk of locoregional recurrence in PTC.^[17–20] These factors are evaluated in preoperative staging US. Therefore, accurate preoperative staging US should be performed for proper treatment and management of PTC patients.^[21]

In the AJCC 8th edition published in 2016, ETE was defined as the presence of gross ETE and distinguishes stage T3 from the other T stages.^[15] This was a major change from the previous AJCC 7th edition where T3 staging was based on the presence of micro ETE in pathology samples.^[22] The reason for this change in T3 staging was that micro ETE was shown not to affect prognosis.^[23–25] Therefore, we used AJCC 8th version TNM staging guidelines and defined ETE as invasion of the strap muscles (sternohyoid, sternothyroid, thyrohyoid, or omohyoid muscles).^[15]

Table 3
Comparison of US features, SWE parameters, and clinicopathologic factors for predicting LNM.

Variable	LNM (+) (n=44)	LNM (-) (n=67)	P value
Age	48.1 ± 15.1	49.4 ± 9.8	.62
Sex			.009
Male	18	12	
Female	26	55	
Surgery			.003
Subtotal thyroidectomy or lobectomy	27	58	
Total thyroidectomy	17	9	
Size (group)			.012
<10 mm	18	44	
≥10 mm	26	23	
Composition			.65
Solid	42	65	
Mixed	2	2	
Echogenicity			.43
Iso	2	6	
Hypo	35	45	
Marked hypo	7	16	
Margin			.19
Circumscribed	8	20	
Irregular	36	47	
Microcalcification			.23
No	14	30	
Yes	30	37	
Shape			1.0
Wider than tall	16	24	
Taller than wide	28	43	
ATA US pattern			.53
Low	0	2	
Indeterminate	4	9	
High	40	56	
T stage on US			.003
T1 (absence of ETE)	21	51	
T3 (presence of ETE)	23	16	
N stage on US			.14
NO	33	58	
N1a/1b	11	9	
E _{max} (kPa)	63.6 ± 45.1	64.0 ± 41.0	.96
E _{mean} (kPa)	48.5 ± 34.7	49.2 ± 29.4	.90
E _{min} (kPa)	28.7 ± 25.2	31.9 ± 21.2	.46
E _{ratio}	5.6 ± 7.7	4.4 ± 3.5	.29

E_{max} = maximum value for a fixed 2-mm diameter circular ROI placed in the stiffest area, E_{mean} = mean value for the ROI, E_{min} = minimum value for the ROI.

Continuous variables are expressed as means ± standard deviations.

In our study, we demonstrated that T3 staging on US (OR = 6.0; $P = .001$) and taller-than-wide shape (OR = 3.4; $P = .035$) were independent predictive factors of ETE on preoperative US. In 1 previous study of 126 patients, T staging on US was found as an independent predictive factor of ETE (OR = 3.809; $P = .005$), consistent with our study.^[26] However, no prior study has directly studied the relationship between malignant features on US and ETE. In our study, we demonstrated that a taller-than-wide shape on US was an independent predictive factor of ETE. Nodule size was significantly higher in the group with ETE than the group without ETE in a univariate analysis ($P = .036$), but not in a multivariate analysis ($P = .30$). This is consistent with the previous studies of 208 patients (OR = 1.028; $P = .412$)^[21] and 126 patients (OR = 1.172; $P = .063$).^[26]

Table 4
Identification of independent clinical and radiological factors predictive of LNM using multiple regression analysis.

Variables	OR	95% CI	P value
Sex			.012
Male	Ref		
Female	3.0	1.2, 8.7	
Size	1.2	0.52, 3.1	.60
Surgery			.020
Subtotal thyroidectomy or lobectomy	Ref		
Total thyroidectomy	3.3	1.2, 9.2	
T stage on US			.027
T1 (absence of ETE)	Ref		
T3 (presence of ETE)	3.0	1.2, 8.1	

95% CI = 95% confidence interval, OR = odds ratio, Ref. = reference.

Elastography was recently shown to complement B-mode US in patients with thyroid cancer and distinguish benign from malignant thyroid nodules.^[27–29] SWE is a relatively new elastography technique, and unlike static elastography, is operator-independent.^[30] In addition, SWE has the advantage of being more objective because quantitative elasticity parameters are calculated automatically in contrast to static elastography.^[30,31] SWE is divided into point SWE and 2-dimensional SWE (2-D SWE), and 2-D SWE is divided into “One-Shot” SWE and “Real-time” technique.^[32] In our study, we used “Real-time” 2-D SWE technique among them.

Our findings, however, indicate that SWE quantitative elasticity parameters were not predictive factors of ETE in patients with PTC. In addition, each of the 4 elasticity parameters (E_{max}, E_{mean}, E_{min}, and E_{ratio}) had a lower diagnostic performance than B-mode US alone for predicting ETE. When elasticity parameters were combined with B-mode US parameters, specificity increased but without statistical significance. However, sensitivity, PPV, NPV, accuracy, and AUC decreased. Park et al^[21] reported that E_{mean} (OR = 1.009; $P = .032$) and E_{min} (OR = 1.001; $P = .0488$) were independent predictors of ETE, inconsistent with the results of our study. Also, in that study, elasticity parameters were higher in the group with ETE than in the group without ETE.^[21] However, in our study, although not statistically significant, all 4 elasticity parameters in the group with ETE were lower than those in the group without ETE. The elasticity of PTC depends on the composition of the stroma, and it is known that the more collagen present in stroma, the higher the elasticity value.^[33] However, it is still unclear whether the higher the T staging is proportional to a higher elasticity. One possible explanation for this result is that the higher the T stage, the more the degree of tumor necrosis, and thus the lower the elasticity value.

Our results also indicated that SWE elasticity parameters were not independent predictive factors of LNM. Several previous studies have showed that direct measurement of SWE parameters can help distinguish benign from malignant tumors in patients with cervical LNM.^[34,35] Park et al^[36] reported that SWE parameters of PTCs could predict cervical LNM which was discordant with our study. In more detail, Park et al^[36] found that central LNM was related to E_{mean} (OR = 1.006; $P = .037$) and E_{max} (OR = 1.005; $P = .037$), and lateral LNM was related to E_{min} (OR = 1.017; $P = .015$). In addition, elasticity parameter values were higher in the LNM group than the nonLNM group, whereas in our study, only E_{ratio} was slightly higher in the LNM

Table 5
Comparison of the diagnostic performance of US T-staging and elasticity parameters for ETE.

	Cut-off	SEN	P	SPE	P	PPV	P	NPV	P	Acc	P	AUC	P
US T-staging	≥3	69.7 [23/33]		79.5 [62/78]		59.0 [23/39]		86.1 [62/72]		76.6 [85/111]		0.746	
E _{max}	≤43.2 ^a	48.5 [16/33]	.13	66.7 [52/78]	.10	38.1 [16/42]	.097	75.6 [52/49]	.15	61.3 [68/111]	.020	0.561	.020
E _{mean}	≤30.3 ^a	42.4 [14/33]	.047	73.1 [57/78]	.45	40.0 [14/35]	.16	75.0 [57/76]	.12	64.0 [71/111]	.057	0.568	.023
E _{min}	≤13.1 ^a	36.4 [12/33]	.014	82.1 [64/78]	.84	46.2 [12/26]	.45	75.3 [64/85]	.13	68.5 [76/111]	.23	0.586	.035
E _{ratio}	≤2	27.3 [9/33]	.001	84.6 [66/78]	.53	42.9 [9/21]	.32	73.3 [66/90]	.071	67.6 [75/111]	.18	0.524	.008

a = kilo Pascal (kPa) in unit, Acc = accuracy (%), AUC = area under the curve, E_{max} = maximum value for a fixed 2-mm diameter circular ROI placed in the hardest area, E_{mean} = mean value for ROI, E_{min} = minimum value for ROI, NPV = negative predictive value (%), P=P value, PPV = positive predictive value (%), SEN = sensitivity (%), SPE = specificity (%).

Table 6
Comparison of the diagnostic performance of US T-staging and combined US T-staging with elasticity parameters for ETE.

	SEN	P	SPE	P	PPV	P	NPV	P	Acc	P	AUC	P
US T-staging	69.7 [23/33]		79.5 [62/78]		59.0 [23/39]		86.1 [62/72]		76.6 [85/111]		0.746	
US T-staging + E _{max}	33.3 [11/33]	.007	84.6 [66/78]	.23	47.8 [11/23]	.55	75.0 [66/88]	.11	69.4 [77/111]	.29	0.632	.005
US T-staging + E _{mean}	33.3 [11/33]	.007	83.3 [65/78]	.68	45.8 [11/24]	.45	74.7 [65/87]	.11	68.5 [76/111]	.23	0.635	.008
US T-staging + E _{min}	39.4 [13/33]	.026	82.1 [64/78]	.84	48.2 [13/27]	.54	76.2 [64/84]	.17	69.4 [77/111]	.29	0.629	.004
US T-staging + E _{ratio}	51.5 [17/33]	.421	80.8 [63/78]	.10	53.1 [17/32]	.80	79.7 [63/79]	.39	72.1 [80/111]	.54	0.659	.013

Acc = accuracy (%), AUC = area under the curve (%), E_{max} = maximum value for a fixed 2-mm diameter circular ROI placed in the hardest area, E_{mean} = mean value for ROI, E_{min} = minimum value for ROI, NPV = negative predictive value (%), PPV = positive predictive value (%), SEN = sensitivity (%), SPE = specificity (%).

positive group than in the LNM negative group, but without statistical significance.

In our study, female sex (OR = 3.0; *P* = .012) and T3 staging on preoperative US (OR = 3.0; *P* = .027) were independent predictive factors of LNM. Xu et al^[37] reported that capsule involvement (OR = 20.632; *P* < .001) was an independent predictive factor of LNM in preoperative US. Other previous studies reported similar conclusions.^[38,39] This can be explained by histopathological characteristics such as proximity to the thyroid capsule or vascular invasion.^[40,41] Total thyroidectomy was also an independent predictive factor of LNM. This supports the recommendation that total thyroidectomy should be performed when regional metastasis such as LNM is present.^[3] However, Xu et al^[37] reported that sex (*P* = .097) was not associated with LNM. This discrepancy between the studies is likely due to differences in sex ratios in the studies.

Our study had some limitations. First, our study was retrospective, thus there may have been selection bias. Second, the number of patients in our study was small. Investigation of more patients who are recruited prospectively will allow more conclusive inferences. Third, cervical LNM was not analyzed according to central LNM or lateral LNM. In the AJCC 8th edition, central LNM and lateral LNM are divided into N1a and N1b, respectively. However, because fewer than 5 patients had lateral LNM (of 44 total LNMs), we did not divide patients into central LNM and lateral LNM groups. Finally, we did not analyze inter-reader or intra-reader agreement. However, the focus of our study was on evaluating the diagnostic performance of SWE in terms of prediction of ETE and LNM.

In conclusion, SWE in PTC patients when combined with B-mode US offered no benefits in terms of prediction of ETE and LNM relative to B-mode US alone.

Author contributions

Conceptualization: Yu-Mee Sohn.

Data curation: Dong Yoon Han, Yu-Mee Sohn, Mirinae Seo, Seong Jong Yun, Won Seo Park, Seok Ho Jeon, Yong Hyun Cho.

Formal analysis: Dong Yoon Han, Yu-Mee Sohn, Mirinae Seo, Seong Jong Yun, Won Seo Park, Seok Ho Jeon, Yong Hyun Cho.

Investigation: Dong Yoon Han, Yu-Mee Sohn, Seong Jong Yun.

Methodology: Dong Yoon Han, Yu-Mee Sohn, Seong Jong Yun.

Software: Dong Yoon Han.

Supervision: Dong Yoon Han, Mirinae Seo, Won Seo Park.

Validation: Dong Yoon Han, Won Seo Park, Seok Ho Jeon, Yong Hyun Cho.

Visualization: Dong Yoon Han, Seong Jong Yun.

Writing – original draft: Dong Yoon Han.

Writing – review & editing: Dong Yoon Han, Yu-Mee Sohn, Mirinae Seo, Seok Ho Jeon, Yong Hyun Cho.

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