Original Investigation

Percutaneous Ethanol Injection vs Reoperation for Locally Recurrent Papillary Thyroid Cancer
A Systematic Review and Pooled Analysis

Tatyana E. Fontenot, MD; Ahmed Deniwar, MD; Parisha Bhatia, MD; Zaid Al-Qurayshi, MD; Gregory W. Randolph, MD; Emad Kandil, MD

IMPORTANCE Reoperation for recurrent papillary thyroid cancer (PTC) can be associated with a high rate of complications and failure to provide lasting remission. Percutaneous ethanol injection (PEI) may be an effective nonsurgical management option for locally recurrent PTC.

OBJECTIVE This systematic analysis of the current literature compares the efficacy and complications related to PEI vs reoperative surgical intervention for treatment of locally recurrent PTC.

DATA SOURCES Original studies were identified using the keywords "thyroid/ethanol" and "recurrent thyroid cancer/repeat surgery."

STUDY SELECTION Studies evaluating reoperation or PEI for lymph node metastases in patients with primary surgery of total thyroidectomy with appropriate lymph node dissection where indicated were included in the analysis for both reoperation and PEI. Animal studies, single case reports, and studies with fewer than 10 lesions were excluded.

DATA EXTRACTION AND SYNTHESIS Outcomes included interval to detection of recurrence, success and failure rates, recurrence rates, complication rates, and follow-up duration. Between-group outcome differences were calculated using random-effects models, and pooled data cross-tabulation and logistic regression analysis were used.

RESULTS In all, 945 publications were identified, and 27 studies met the inclusion criteria. There were no studies that directly compared the 2 treatment techniques. A total of 1617 patients were included in this analysis; 168 (11.4%) were treated with PEI, and 1449 (88.6%) were treated with reoperation. Reoperation was successful in 94.8% of cases compared with an 87.5% success rate for PEI (odds ratio [OR], 2.58; 95% CI, 1.55-4.31; $P < .001$). The recurrence rates for PEI and reoperation at the site of the treated lesion or elsewhere in the neck were also similar (OR, 1.07; 95% CI, 0.65-1.77; $P = .78$). Reoperation was associated with a 3.5% pooled risk of complications, while PEI incurred a pooled risk of 1.2% (OR, 2.9; 95% CI, 0.72-12.3; $P = .08$). However, most studies did not report routine preoperative and postoperative laryngoscopies, an evaluation needed for accurate neural complication analysis associated with each procedure.

CONCLUSIONS AND RELEVANCE High-quality, well-designed studies are needed to evaluate the feasibility of incorporating PEI into the treatment protocol of PTC. Although presently inferior to reoperation, PEI has the potential to be a widely accepted and effective nonsurgical treatment option for limited recurrent PTC in poor surgical candidates or patients seeking to avoid multiple reoperations.

JAMA Otolaryngol Head Neck Surg. 2015;141(6):512-518. doi:10.1001/jamaoto.2015.0596
Published online April 30, 2015. Corrected on July 13, 2015.

Author Affiliations: Department of Surgery, Tulane University School of Medicine, New Orleans, Louisiana (Fontenot, Deniwar, Bhatia, Kandil); School of Public Health and Tropical Medicine, Tulane University, New Orleans, Louisiana (Al-Qurayshi); Division of Thyroid and Parathyroid Surgery, Department of Otolaryngology, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts (Randolph); Division of Surgical Oncology, Department of Surgery, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts (Randolph); Department of Otolaryngology, Tulane University School of Medicine. New Orleans, Louisiana (Kandil).

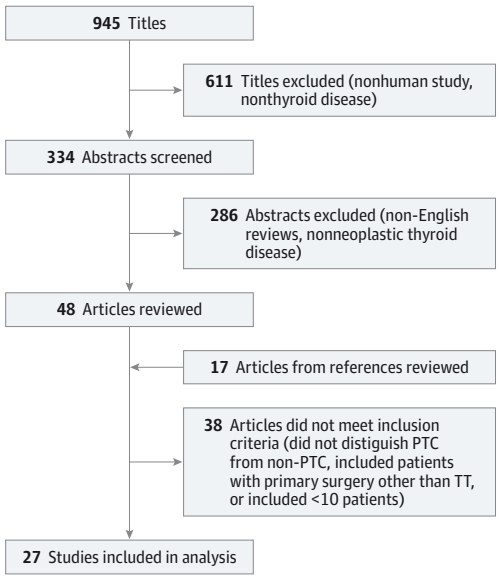
Corresponding Author: Emad Kandil, MD, Tulane Department of Surgery, Department of Otolaryngology, 1430 Tulane Ave, SL 59, New Orleans, LA 70112 (ekandil@tulane.edu)

Papillary thyroid cancer (PTC) is the most common malignant condition of the thyroid and has an overall 10-year survival rate of greater than 90%.[1] However, nodal recurrence rates can be high, especially in patients with macroscopic nodal metastases at first presentation.[2] This risk has been reported to be as high as 30% to 40%, even after appropriately aggressive initial lymph node dissection during the primary surgery.[3-6] And while surgical resection is regarded as the standard treatment for recurrence, rates of remission after reoperation range from 19% to 67%, depending the exact definition of remission.[7,8] Furthermore, reoperation for locally recurrent PTC continues to present a risk of complications greater than that for primary surgery. While the risk of recurrent laryngeal nerve (RLN) injury in primary surgery is reported to be 0% to 3%, for reoperation this risk can be as high as 12%.[9,10]

Percutaneous ethanol injection (PEI) is a treatment technique that may be able to treat PTC lesions with an acceptable degree of efficacy while avoiding most of the complications of surgical intervention.[11,12] However, to our knowledge, there are no large, high-quality studies to provide unequivocal conclusions regarding efficacy of PEI.

The first aim of our study is to compare the corresponding PTC-specific end points of PEI and reoperation in the existing literature and draw a preliminary conclusion regarding PEI's efficacy in achieving immediate control of locally recurrent metastatic disease. Our second aim is to elucidate the biggest obstacles to a fair comparison of the 2 procedures that prevent firm recommendations regarding the use of PEI and reoperation in treatment of recurrent PTC.

Figure. Literature Search and Study Selection Process



Nonhuman studies included in vivo proof-of-concept and safety trials in laboratory animals; nonthyroid disease included hepatic or melanoma lesions; nonneoplastic thyroid disease included hot or cold benign thyroid nodules, multinodular goiter, Graves disease, and colloid cyst; fewer than 10 patients refers to studies with fewer than 10 patients or individually treated lesions (applicable to percutaneous ethanol injection studies only). PTC indicates papillary thyroid carcinoma; TT, total thyroidectomy.

Methods

Literature Search

A literature search of PubMed, EMBASE, the Cochrane Library, and ClinicalTrials.gov was performed independently by 2 investigators. To identify all work concerning PEI in treatment of thyroid cancer, all databases but PubMed were queried with the search terms "thyroid, ethanol"; for PubMed, the search term "thyroid, ethanol ablation" was used for more precise results. Subsequently, search terms "recurrent, thyroid cancer, repeat surgery" were applied to the same set of databases.

Prospective and high-quality retrospective cohort studies and case series were included in the study. All titles available by January 2014 were reviewed. Non-English language manuscripts, scientific literature reviews, animal studies, single case reports, and studies with fewer than 10 locally recurrent PTC lesions were excluded. Only patients with a diagnosis of PTC and prior primary surgery of single or staged total thyroidectomy with appropriate lymph node dissection where indicated were included in the analysis.

Outcomes evaluated included intervals to detection of recurrence, retreatment success rates, change in thyroglobulin (Tg) serum levels, recurrence rates, complication rates, and follow-up duration. Ultrasonography was the most commonly used technique to monitor outcome of treatment. Successful treatment by PEI was defined as shrinkage of the lesion by 50% or greater on follow-up ultrasonography and no evidence of new growth within the lesion. Failure of PEI was defined as any growth in a PEI-treated PTC lesion. Successful reoperation was defined as a complete resection of the nidus of metastatic disease in a previously dissected or uninvolved neck compartment as demonstrated by postoperative follow-up ultrasonography. Reoperation failures were any incomplete resections, except for cases in which incomplete resection was required to preserve RLN function.

In both treatment techniques, recurrences were defined as any new PTC lesions in the cervical region or in distant sites identified by routine monitoring (ultrasonography, computed tomography [CT], positron emission tomography [PET], or radioiodine scan).

Analysis

Systematic analysis was performed on pooled raw data, including total number of patients, successfully treated patients, patients with recurrences, and instances of complications. These outcomes data were transcribed in tabular form. Between-group outcome differences were calculated using random-effects models and logistic regression analysis. The Wilcoxon rank-sum test was applied for testing the differences in Tg serum level values between the 2 study groups. Outcomes calculated were univariate owing to lack of data regarding confounding factors, which prevented control for these variables. Heterogeneity could not be assessed from the available data.

Table 1. Study and Patient Population Characteristics

Source	Study Design	LOE	Age Range at Initial Diagnosis, y	Age Range at Recurrence, y	Mean Interval to Recurrence Detection, mo
Reoperation					
Lang et al,[13] 2013, China	Retrospective	3	11.8-85.3	12.1-87.4	33.6
Uchida et al,[5] 2013, Japan	Retrospective cohort	2b	NR	10-87	NR
Young et al,[14] 2013, United States	Retrospective cohort	2b	NR	NR	8.7
Hughes et al,[8] 2012, United States	Retrospective cohort	2b	16.6-75	20-77	24.7
Tufano et al,[1] 2012, United States	Retrospective	3	NR	16-84	36
Yim et al,[15] 2011, South Korea	Retrospective	3	NR	18-75	27
Clayman et al,[16] 2011, United States	Retrospective	3	9-79	12-82	21
Al-Saif et al,[17] 2010, United States	Retrospective	3	15-71	18-73	36
Erbil et al,[18] 2010, Turkey	Prospective	1b	10-55	14-61	56.4
Ilgan et al,[19] 2010, Turkey	Prospective	1b	18-68	NR	NR
Shen et al,[20] 2010, United States	Retrospective	3	NR	NR	NR
Alvarado et al,[21] 2009, Australia	Retrospective cohort	2b	NR	NR	NR
Roh et al,[22] 2009, South Korea	Prospective	1b	NR	16-85	62.4
Sippel et al,[23] 2008, United States	Prospective	1b	NR	NR	61
Farrag et al,[24] 2007, United States	Retrospective	3	10-58	15-63	60
McCoy et al,[25] 2007, United States	Retrospective cohort	2b	NR	22-73	NR
Stulak et al,[26] 2006, United States	Retrospective cohort	2b	NR	5-90	10
Roh et al,[27] 2006, South Korea	Retrospective cohort	2b	24-71	29-76	62.4
Karwowski et al,[28] 2002, United States	Retrospective case series	4	NR	29-65	NR
Alzahrani et al,[29] 2002, Saudi Arabia	Retrospective cohort	2b	NR	20-60	NR
Percutaneous Ethanol Injection					
Guenette et al,[30] 2013, United States	Retrospective case series	4	NR	30-85	NR
Hay et al,[11] 2013, United States	Prospective	1b	31-69	47-73	78
Heilo et al,[12] 2011, Norway	Retrospective	3	20-76	21-85	24
Kim et al,[31] 2008, South Korea	Retrospective	3	NR	19-80	NR
Lim et al,[32] 2007, South Korea	Prospective	1b	NR	31-74	NR
Monchik et al,[33] 2006, United States	Retrospective case series	4	NR	39-78	NR
Lewis et al,[34] 2002, United States	Prospective	1b	NR	27-83	53

Abbreviations: LOE, level of evidence; NR, not reported.

Results

Our literature search for studies evaluating reoperation returned a total of 300 titles; our search for PEI resulted in 645 titles; together the 2 searches returned a total of 945 source titles for review of PEI and reoperation (**Figure**). There were no studies that directly compared the 2 treatment techniques. A total of 611 titles featuring animal studies or nonthyroid disease were excluded. Abstracts were reviewed and 286 reviews and studies were excluded for lack availability of English-language report and lack of focus on nonneoplastic thyroid disease. Forty-eight texts were closely evaluated to exclude those studies that did not distinguish between PTC and non-PTC thyroid cancers (23 studies), included patients with primary surgery other than total thyroidectomy (8 studies), and those with fewer than 10 patients (4 studies). Three of the reviewed studies appeared in more than 1 database collection and were counted only once. Seventeen full texts of relevant referenced studies were reviewed. Nineteen of the originally considered titles and 8 of the reviewed references met inclusion criteria, for a total of 27 studies included in the final analysis.

A total of 1617 patients with recurrent PTC were included in this systematic analysis. Percutaneous ethanol injection was used to treat 270 metastatic PTC lesions in 168 patients (11.4%). Reoperation was used to treat 1449 patients (88.6%) for dissection of the involved compartment. (Because the surgical approach requires en bloc removal of all lymph nodes in a series, total number of lymph nodes resected is rarely reported. Therefore, "number of lesions" could not be analyzed for the reoperation approach.) **Table 1** and **Table 2** list the characteristics of the included studies and the patient populations they evaluated. Median percentage of patients with lymph node involvement at the time of the initial thyroidectomy was 66.0% in studies evaluating reoperation and 73% in PEI studies. Patients in the reoperation group of studies had undergone a median of 1.3 prior reoperations for metastatic lymph node; patients in PEI studies had been operated on a median of 2.1 times before attempting PEI treatment. The interval to detection available in 12 studies evaluating reoperation for recurrent PTC showed a median of 36 months (range, 8-62.4 months) from the time of initial surgery. In studies evaluating PEI, this period was a median of 53 months (range, 24-78 months), but for PEI, the data were available in only 3 studies.

Table 2. Patient and Treatment Characteristics of the Study Population

Source	LN Disease at Initial Presentation, %	Prior Reoperations, Mean No.	Diagnostic Technique	Clinical Events, %		
				Successful Treatment	Complications	Recurrence
Reoperation						
Lang et al[13] (n = 81)	80.2	NR	FNA	100	NR	NR
Uchida et al[5] (n = 56)	NR	0	NA	71	16	13
Young et al[14] (n = 222)	71	NR	NA	95	NR	6
Hughes et al[8] (n = 61)	61	0	FNA	93	15	21
Tufano et al[1] (n = 120)	NR	0.26	FNA	100	27	0
Yim et al[15] (n = 83)	67.5	NR	FNA	84	0	16
Clayman et al[16] (n = 210)	66	NR	FNA	100	1	23
Al-Saif et al[17] (n = 70)	74.3	NR	FNA	17	1	0
Erbil et al[18] (n = 46)	41	1.3	FNA	89	11	4
Ilgan et al[19] (n = 8)	50	NR	FNA	100	13	NR
Shen et al[20] (n = 106)	NR	0.5	UltraS	100	32	29
Alvarado et al[21] (n = 23)	NR	NR	UltraS	100	30	NR
Roh et al[22] (n = 21)	NR	NR	FNA	100	33	NR
Sippel et al[23] (n = 10)	NR	2.6	FNA	100	0	NR
Farrag et al[24] (n = 94)	NR	1.3	FNA	94	15	0
McCoy et al[25] (n = 88)	NR	NR	FNA	88	NR	NR
Stulak et al[26] (n = 100)	NR	2	FNA	100	NR	NR
Roh et al[27] (n = 100)	NR	NR	FNA	100	32	9
Karwowski et al[28] (n = 100)	NR	2.1	FNA	100	0	NR
Alzahrani et al[29] (n = 38)	62	NR	FNA	38	NR	19
Percutaneous Ethanol Injection						
Guenette et al[30] (n = 14)	NR	NR	FNA	93	0	36
Hay et al[11] (n = 25)	68	1.6	FNA	92	0	24
Heilo et al[12] (n = 66)	73	NR	FNA	79	0	3
Kim et al[31] (n = 27)	100	2.1	FNA	96	0	7
Lim et al[32] (n = 16)	NR	NR	FNA	100	6	6
Monchik et al[33] (n = 6)	NR	NR	FNA	83	17	33
Lewis et al[34] (n = 14)	NR	2.1	FNA	86	0	14

Abbreviations: Dx, method of diagnosis; FNA, fine-needle aspiration biopsy; LN, lymph node; NA, not applicable; NR, not reported; UltraS, ultrasonography.

Most metastases were identified by routine screening ultrasonography (26 of 27 studies) with fine-needle aspiration biopsy (FNA) confirmation (22 of 26 studies). The average number of lymph nodes resected during reoperation was 10.05. The average number of lymph nodes treated in studies examining PEI was 1.6 per patient. The mean (SD) estimated initial volume of the treated lymph nodes was 0.45 (0.19) mL.

Based on the analysis of the pooled data, surgery was successful in 94.8% of studied cases compared with an 87.5% success rate for PEI treatment (odds ratio [OR], 2.58; 95% CI, 1.55-

Table 3. Locations of PEI-Treated and Resected Lymph Nodes

	Treated Lymph Nodes, %	
Neck Compartment	PEI	Reoperation
Central	35	48
Lateral	59	40
Undefined	6	12

Abbreviation: PEI, percutaneous ethanol injection.

4.31; $P < .001$). The PEI pooled PTC risk of recurrence at the site of the treated lesion or elsewhere in the neck was 11.9%; the recurrence rate for patients who underwent a reoperation was 12.7% (OR, 1.07; 95% CI, 0.65-1.77; $P = .78$). Surgery was associated with a 3.5% pooled risk of complications, while PEI incurred a pooled risk of 1.2% (OR, 2.9; 95% CI, 0.72-12.3; $P = .08$). However, uneven distribution of the treated lymph nodes in central and lateral compartments complicates this comparison (**Table 3**).

The mean Tg serum levels in PEI studies ranged from 0.7 to 9.2 ng/mL compared with those of reoperation studies, which ranged from 3.2 to 431 ng/mL ($P = .02$) (**Table 4**). Post-PEI Tg serum levels ranged from 0.2 to 2.8 ng/mL compared with reoperation postoperative Tg serum levels of 0.3 to 127.5 ng/mL ($P = .01$). Two of the 5 PEI studies and 4 of 10 reoperation studies demonstrated Tg serum level decline of greater than 75% after treatment. The overall difference in Tg serum level change was not significantly different between the 2 groups. While 3 studies evaluating reoperation demonstrated a Tg level rise of 15% to 151% due to extreme outliers in those data sets, the other 7 demonstrated a postoperative decline of 31% to 98% and an overall median decline of 73%; PEI studies demonstrated a decline of 28% to 97% (median decline, 71%) ($P = .67$).

The mean (SD) follow-up period during which ultrasonography was performed in studies evaluating reoperation was 31.1 (24.6) months, while for PEI it was 32.9 (14.7) months.

Discussion

Based on the presently available data regarding reoperation and PEI for locally recurrent PTC, reoperation is superior to PEI. While PEI treatment shows potential in specific populations, the failure and recurrence rates are significantly higher than those for reoperation. Reoperation should remain the standard of care for recurrent PTC.

Reoperation carries significantly higher complication risk than primary surgery, but it can still provide highly successful outcomes both in terms of low rate of complications and low risk of recurrence.[3] Selective resection of the macroscopically neoplastic lymph node is contrary to the standard of oncologic reoperation, which requires complete removal of all lymph nodes in the involved area of the neck to be considered a successful reoperation. The PEI procedure can be applied only to small metastases and represents a nonsurgical, minimally invasive, "berry picking" intervention. Long-term follow-up of such limited treatment may reveal the same recurrence rate that has been associated with surgical berry picking. Studies focused on PEI have not required complete disappearance of the lesion to consider the treatment successful. The fact that cancer in the potentially persistently affected tissue remains detectable makes the comparison of PEI and reoperation fundamentally difficult.

There are differences in patient populations undergoing the different treatments due to deliberate selection bias. Studies evaluating reoperation have included patients with larger lesions, a greater number of lesions, and particularly aggressive PTC.[1,2] The investigators leading the studies examining PEI tend to select poor surgical candidates with a limited number of cervical lesions. Selection bias is evident from the respective mean numbers of treated lymph nodes: 10.05 for patients undergoing reoperation vs 1.5 for those treated with PEI. Patients treated with PEI had a comparable number of previous surgeries, but the older median age of these patients suggests indolent recurrent disease rather than an aggressive pattern of growth. Patients undergoing reoperation clearly carried a higher disease burden and consequently an increased risk of failure and recurrence.

Comparison of complications of the 2 techniques is also complicated. Few of the studies make a distinction between treatments of the central and lateral compartments of the neck. The PEI procedure was chiefly used to treat lateral neck lymph nodes, where risk of RLN injury is minimal; the data regarding this complication is skewed in PEI's favor. To balance the comparison of RLN injury risk associated with either treatment, future investigations should consider reoperation and PEI in the central compartment separately from those in the lateral compartment. Furthermore, while most of the studies included a discussion of RLN injury, few discussed the use of routine pretreatment and posttreatment laryngoscopy in determining presence of vocal cord dysfunction.

Decline in Tg serum levels is an indicator of adequate reoperation or PEI treatment of macrometastases, even in the setting of multiple prior recurrences.[3,8,11] While patients who underwent reoperation had significantly higher initial and postoperative Tg levels, comparison of the Tg serum level trends indicates that the 2 techniques have a very similar effect on the posttreatment Tg serum levels. It should be noted that assays used to measure Tg levels have undergone refinements in the examined period. In addition, while some studies report baseline levels only, several of the newer studies instead featured stimulated levels. This further complicates the comparison. Radioactive iodine, CT, or PET or scans were used to monitor for distant metastases in several studies evaluating reoperation, but significantly fewer PEI studies than reoperation studies discuss the use of these imaging procedures.

Review of these studies revealed that routine postoperative screening with ultrasonography and FNA has become a ubiquitous component of PTC treatment. Nearly all studies directly stated that this protocol identified the locally recurrent lesions. Likewise, measurement of Tg levels appears to be gaining acceptance among clinicians treating PTC, although the data on this metric are not yet as abundant. Evaluation of vocal cords and imaging techniques used in screening for distant metastases are 2 aspects of PTC care that could benefit from a similarly systematic approach. While large, randomized prospec-

Table 4. Patient Serum Thyroglobulin Levels Before and After Study Treatment

Source[a]	Mean Thyroglobulin Level, ng/mL		Mean Follow-up Duration, mo
	Pretreatment	Posttreatment	
Reoperation			
Lang et al[13]	4.9	12.3	NR
Uchida et al[5]	NR	NR	NR
Young et al[14]	NR	NR	66.2
Hughes et al[8]	20.7	0.41	15.5
Tufano et al[1]	3.2	0.3	41.5
Yim et al[15]	18.32	3.3	64.8
Clayman et al[16]	NR	NR	87
Al-Saif et al[17]	8.4	9.7	60
Erbil et al[18]	12.7	16.3	NR
Ilgan et al[19]	431	113.7	1.5
Shen et al[20]	NR	NR	NR
Alvarado et al[21]	NR	NR	3
Roh et al[22]	NR	NR	NR
Sippel et al[23]	23.7	NR	NR
Farrag et al[24]	NR	NR	24
McCoy et al[25]	44.4	12.5	19
Stulak et al[26]	NR	NR	30
Roh et al[27]	37	3.7	32
Karwowski et al[28]	NR	NR	NR
Alzahrani et al[29]	184.8	127.5	20.7
Percutaneous Ethanol Injection			
Guenette et al[30]	9.22	0.3	38.5
Hay et al[11]	3.9	2.8	65
Heilo et al[12]	0.7	0.2	38.4
Kim et al[31]	NR	NR	27.7
Lim et al[32]	2.53	0.2	24
Monchik et al[33]	6.1	2	18.7
Lewis et al[34]	NR	NR	18

Abbreviation: NR, not reported.

[a] See Table 2 for sample sizes.

tive studies may not be feasible for evaluation of every new intervention, adherence to a rational treatment protocol may allow for a relatively easy retrospective comparison to standard of care.

The PEI procedure may offer significant health care expenditure savings because it does not need to be performed in the operating room, does not require general anesthesia, and is unlikely to require a significant period of inpatient observation. The benefit of PEI in a single treated lesion may not be permanent, and patients may require repeated treatments. This reality is suggested by the recurrence risk of 11.9% after PEI in the examined studies. In contrast, the median disease-free period following adequately aggressive reoperations can be as long as 7.25 years.[16] Therefore, while PEI may represent a promising treatment in high-risk patients with recurrent PTC, most of the current literature supports reoperation as the standard of clinical care. Based on available data, our recommendations include routine pretreatment and posttreatment laryngoscopy, measurement of Tg levels, and routine monitoring for recurrent disease with follow-up measurement of Tg levels, ultrasonography, with FNA.

Conclusions

In practiced hands, surgery is the indisputable standard of care for recurrent PTC recurrences. While PEI is a minimally invasive, it cannot provide definitive treatment for recurrent PTC. Further high-quality investigation is needed to establish PEI's role in the treatment of high-risk patients who have few viable options for treatment, whether the intent is curative or palliative. The characteristics of PEI make it a potential complement to reoperation in the management of recurrent PTC. Routine evaluation of RLN function and Tg levels as well as ultrasonography with FNA in patients treated with either reoperation or PEI will provide a high standard of care immediately and generate high-quality data to compare their outcomes in future studies.

ARTICLE INFORMATION

Submitted for Publication: August 2, 2014; final revision received March 2, 2015; accepted March 18, 2015.

Published Online: April 30, 2015. doi:10.1001/jamaoto.2015.0596.

Author Contributions: Drs Randolph and Kandil had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Fontenot, Al-Qurayshi, Randolph, Kandil.
Acquisition, analysis, or interpretation of data:

Fontenot, Deniwar, Bhatia, Al-Qurayshi, Randolph.
Drafting of the manuscript: Fontenot, Bhatia, Randolph, Kandil.
Critical revision of the manuscript for important intellectual content: Fontenot, Deniwar, Al-Qurayshi, Randolph, Kandil.
Statistical analysis: Fontenot, Bhatia, Al-Qurayshi.
Administrative, technical, or material support: Randolph, Kandil.
Study supervision: Randolph, Kandil.

Conflict of Interest Disclosures: None reported.

Previous Presentation: This research was presented as a poster at the 2014 International Federation of Head and Neck Oncologic Societies–American Head and Neck Society annual meeting; July 26, 2014; New York, New York.

Correction: This article was corrected on July 13, 2015, to fix a misspelled author's name.

REFERENCES

1. Tufano RP, Bishop J, Wu G. Reoperative central compartment dissection for patients with recurrent/persistent papillary thyroid cancer: efficacy, safety, and the association of the BRAF mutation. *Laryngoscope*. 2012;122(7):1634-1640.

2. Randolph GW, Duh QY, Heller KS, et al; American Thyroid Association Surgical Affairs Committee's Taskforce on Thyroid Cancer Nodal Surgery. The prognostic significance of nodal metastases from papillary thyroid carcinoma can be stratified based on the size and number of metastatic lymph nodes, as well as the presence of extranodal extension. *Thyroid*. 2012;22(11):1144-1152.

3. Phelan E, Kamani D, Shin J, Randolph GW. Neural monitored revision thyroid cancer surgery: surgical safety and thyroglobulin response. *Otolaryngol Head Neck Surg*. 2013;149(1):47-52.

4. Grigsby PW, Reddy RM, Moley JF, Hall BL. Contralateral papillary thyroid cancer at completion thyroidectomy has no impact on recurrence or survival after radioiodine treatment. *Surgery*. 2006;140(6):1043-1047.

5. Uchida H, Imai T, Kikumori T, et al. Long-term results of surgery for papillary thyroid carcinoma with local recurrence. *Surg Today*. 2013;43(8):848-853.

6. Alzahrani AS, Xing M. Impact of lymph node metastases identified on central neck dissection (CND) on the recurrence of papillary thyroid cancer: potential role of BRAFV600E mutation in defining CND. *Endocr Relat Cancer*. 2013;20(1):13-22.

7. Park J, Lim JA, Kim TH, et al. Serum thyroglobulin level measured after thyroxine withdrawal is useful to predict further recurrence in whole body scan-negative papillary thyroid cancer patients after reoperation. *Endocr J*. 2012;59(11):1021-1030.

8. Hughes DT, Laird AM, Miller BS, Gauger PG, Doherty GM. Reoperative lymph node dissection for recurrent papillary thyroid cancer and effect on serum thyroglobulin. *Ann Surg Oncol*. 2012;19(9):2951-2957.

9. Harari A, Sippel RS, Goldstein R, et al. Successful localization of recurrent thyroid cancer in reoperative neck surgery using ultrasound-guided methylene blue dye injection. *J Am Coll Surg*. 2012;215(4):555-561.

10. Roh JL, Kim JM, Park CI. Central compartment reoperation for recurrent/persistent differentiated thyroid cancer: patterns of recurrence, morbidity, and prediction of postoperative hypocalcemia. *Ann Surg Oncol*. 2011;18(5):1312-1318.

11. Hay ID, Lee RA, Davidge-Pitts C, Reading CC, Charboneau JW. Long-term outcome of ultrasound-guided percutaneous ethanol ablation of selected "recurrent" neck nodal metastases in 25 patients with TNM stages III or IVA papillary thyroid carcinoma previously treated by surgery and 131I therapy. *Surgery*. 2013;154(6):1448-1454.

12. Heilo A, Sigstad E, Fagerlid KH, et al. Efficacy of ultrasound-guided percutaneous ethanol injection treatment in patients with a limited number of metastatic cervical lymph nodes from papillary thyroid carcinoma. *J Clin Endocrinol Metab*. 2011;96(9):2750-2755.

13. Lang BH, Wong KP, Wan KY. Postablation stimulated thyroglobulin level is an important predictor of biochemical complete remission after reoperative cervical neck dissection in persistent/recurrent papillary thyroid carcinoma. *Ann Surg Oncol*. 2013;20(2):653-659.

14. Young S, Harari A, Smooke-Praw S, Ituarte PHG, Yeh MW. Effect of reoperation on outcomes in papillary thyroid cancer. *Surgery*. 2013;154(6):1354-1361.

15. Yim JH, Kim WB, Kim EY, et al. The outcomes of first reoperation for locoregionally recurrent/persistent papillary thyroid carcinoma in patients who initially underwent total thyroidectomy and remnant ablation. *J Clin Endocrinol Metab*. 2011;96(7):2049-2056.

16. Clayman GL, Agarwal G, Edeiken BS, Waguespack SG, Roberts DB, Sherman SI. Long-term outcome of comprehensive central compartment dissection in patients with recurrent/persistent papillary thyroid carcinoma. *Thyroid*. 2011;21(12):1309-1316.

17. Al-Saif O, Farrar WB, Bloomston M, Porter K, Ringel MD, Kloos RT. Long-term efficacy of lymph node reoperation for persistent papillary thyroid cancer. *J Clin Endocrinol Metab*. 2010;95(5):2187-2194.

18. Erbil Y, Sari S, Ağcaoğlu O, et al. Radio-guided excision of metastatic lymph nodes in thyroid carcinoma: a safe technique for previously operated neck compartments. *World J Surg*. 2010;34(11):2581-2588.

19. Ilgan S, Oztürk E, Yildiz R, et al. Combination of preoperative ultrasonographic mapping and radioguided occult lesion localization in patients with locally recurrent/persistent papillary thyroid carcinoma: a practical method for central compartment reoperations. *Clin Nucl Med*. 2010;35(11):847-852.

20. Shen WT, Ogawa L, Ruan D, et al. Central neck lymph node dissection for papillary thyroid cancer: comparison of complication and recurrence rates in 295 initial dissections and reoperations. *Arch Surg*. 2010;145(3):272-275.

21. Alvarado R, Sywak MS, Delbridge L, Sidhu SB. Central lymph node dissection as a secondary procedure for papillary thyroid cancer: Is there added morbidity? *Surgery*. 2009;145(5):514-518.

22. Roh JL, Yoon YH, Park CI. Recurrent laryngeal nerve paralysis in patients with papillary thyroid carcinomas: evaluation and management of resulting vocal dysfunction. *Am J Surg*. 2009;197(4):459-465.

23. Sippel RS, Elaraj DM, Poder L, Duh QY, Kebebew E, Clark OH. Localization of recurrent thyroid cancer using intraoperative ultrasound-guided dye injection. *World J Surg*. 2009;33(3):434-439.

24. Farrag TY, Agrawal N, Sheth S, et al. Algorithm for safe and effective reoperative thyroid bed surgery for recurrent/persistent papillary thyroid carcinoma. *Head Neck*. 2007;29(12):1069-1074.

25. McCoy KL, Yim JH, Tublin ME, Burmeister LA, Ogilvie JB, Carty SE. Same-day ultrasound guidance in reoperation for locally recurrent papillary thyroid cancer. *Surgery*. 2007;142(6):965-972.

26. Stulak JM, Grant CS, Farley DR, et al. Value of preoperative ultrasonography in the surgical management of initial and reoperative papillary thyroid cancer. *Arch Surg*. 2006;141(5):489-494.

27. Roh JL, Park JY, Rha KS, Park CI. Is central neck dissection necessary for the treatment of lateral cervical nodal recurrence of papillary thyroid carcinoma? *Head Neck*. 2007;29(10):901-906.

28. Karwowski JK, Jeffrey RB, McDougall IR, Weigel RJ. Intraoperative ultrasonography improves identification of recurrent thyroid cancer. *Surgery*. 2002;132(6):924-928.

29. Alzahrani AS, Raef H, Sultan A, et al. Impact of cervical lymph node dissection on serum TG and the course of disease in TG-positive, radioactive iodine whole body scan-negative recurrent/persistent papillary thyroid cancer. *J Endocrinol Invest*. 2002;25(6):526-531.

30. Guenette JP, Monchik JM, Dupuy DE. Image-guided ablation of postsurgical locoregional recurrence of biopsy-proven well-differentiated thyroid carcinoma. *J Vasc Interv Radiol*. 2013;24(5):672-679.

31. Kim BM, Kim MJ, Kim EK, Park SI, Park CS, Chung WY. Controlling recurrent papillary thyroid carcinoma in the neck by ultrasonography-guided percutaneous ethanol injection. *Eur Radiol*. 2008;18(4):835-842.

32. Lim CY, Yun JS, Lee J, Nam KH, Chung WY, Park CS. Percutaneous ethanol injection therapy for locally recurrent papillary thyroid carcinoma. *Thyroid*. 2007;17(4):347-350.

33. Monchik JM, Donatini G, Iannuccilli J, Dupuy DE. Radiofrequency ablation and percutaneous ethanol injection treatment for recurrent local and distant well-differentiated thyroid carcinoma. *Ann Surg*. 2006;244(2):296-304.

34. Lewis BD, Hay ID, Charboneau JW, McIver B, Reading CC, Goellner JR. Percutaneous ethanol injection for treatment of cervical lymph node metastases in patients with papillary thyroid carcinoma. *AJR Am J Roentgenol*. 2002;178(3):699-704.