ORIGINAL ARTICLE

ALGORITHM FOR SAFE AND EFFECTIVE REOPERATIVE THYROID BED SURGERY FOR RECURRENT/PERSISTENT PAPILLARY THYROID CARCINOMA

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Abstract: *Background.* The aim of this study was to review our experience with reoperative thyroid bed surgery (RTBS) for recurrent/persistent papillary thyroid cancer (PTC), and present an algorithm for safe and effective RTBS.

Methods. This is a retrospective study. Records of 33 consecutive patients who underwent RTBS for recurrent/persistent PTC in a previously operated thyroid bed, and were operated upon by the senior author (R.P.T.) July 2001 to January 2006 were reviewed. Reports of the pre- and post-RTBS serum thyroglobulin (TG) levels, the high-resolution thyroid bed ultrasound examination, pre-RTBS FNA cytopathology, as well as the post-RTBS final histopathology were reviewed. Recurrent laryngeal nerve (RLN) monitoring was used for all patients. Reports of the intra-RTBS condition of the RLN and any reported surgical complications were reviewed. In addition, reports of the pre- and post-RTBS fiberoptic laryngoscopy as well as pre- and post-RTBS serum calcium levels were reviewed.

Results. In our study, 33 consecutive patients underwent RTBS for recurrent/persistent PTC with or without lateral neck dissection. In 30 patients, recurrent/persistent PTC was suspected because of rising serum TG levels, interpreted in conjunction with serum anti-TG-antibody titers by the endocrinology service at our institution. Three patients had serum anti-TG antibodies and their disease was detected and FNA confirmed by a regularly scheduled surveillance ultrasound examination. All patients underwent pre-RTBS high-resolution thyroid bed ultrasound examination and FNA for all suspicious masses. All patients had FNA-confirmed PTC in the thyroid bed. All patients had detailed diagrams localizing areas of FNA-confirmed PTC in the thyroid bed provided to the surgeon. In all study patients, post-RTBS histopathologic findings confirmed sites of recurrent/persistent PTC determined by pre-RTBS US guided FNA. All RLNs (53/53) that were at risk were successfully identified. In 3 patients, the RLN was electively resected because of the envelopment by a large paratracheal mass or tumor densely adherent to the RLN insertion point at the cricothyroid region. There was no incidence of unexpected RLN injury, permanent hypocalcemia, or any other surgery-related complication. Post-RTBS serum TG levels were significantly decreased or undetectable in most patients (2 patients had concurrent lung metastases), when compared with pre-RTBS levels. No patient exhibited thyroid bed recurrent/persistent PTC in the post-RTBS period based on semiannual high resolution neck ultrasound examination with a median follow-up of 2 years.

Conclusions. Safe and effective RTBS is based on a multidisciplinary approach that enables the identification and localization of recurrent/persistent PTC. The surgical algorithm for RTBS described, provides a pathway that all endocrine-head and neck surgeons can comfortably utilize to treat this complex

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Papillary thyroid cancer (PTC) accounts for 75% of thyroid cancer in the United States.[1] The extent of primary treatment for PTC consists of total thyroidectomy with neck dissection as indicated.[1] It is reported that subclinical lymph node metastasis in patients with PTC at the time of primary surgical intervention, together with extrathyroidal tumor extension, increase the rate of local recurrence and need for reoperation.[2]

Reoperative thyroid bed surgery (RTBS) has been reported to have a significantly increased incidence of operative complications when compared with primary thyroidectomy, especially recurrent laryngeal nerve (RLN) injury and hypocalcemia.[3,4] It has been argued by some that every effort should be made to avoid central compartment reoperation by performing a definitive and more radical initial treatment.[3] This aggressive initial approach to treating all PTC does not seem warranted and may also lead to significant morbidity. In this review, we present our experience with central compartment reoperation for recurrent/persistent PTC and provide an algorithm for safe and effective RTBS.

MATERIALS AND METHODS

This is a retrospective study. Records of 33 consecutive patients who underwent RTBS for recurrent/persistent PTC in the central neck, and were operated upon by the senior author (R.P.T.) from July 2001 to January 2006 were reviewed. Data were collected through an electronic database after obtaining the approval for this review from the Institutional Review Board. Patients included 13 men and 20 women, and their average age was 41 years. For the entire study group, reports of pre- and post-RTBS serum thyroglobulin (TG) levels were reviewed (28 patients had unstimulated TG levels pre- and postoperatively, while 5 patients had stimulated TG levels pre- and postoperatively). Pre- and post-RTBS high-resolution neck ultrasound examination reports, pre-RTBS fine needle aspiration (FNA) cytopathology reports, and post-RTBS final histopathologic reports were reviewed. In addition, reports of the intra-RTBS condition of the RLN, and any reported surgical complications were reviewed. Reports of pre- and post-RTBS fiberoptic laryngoscopy as well as pre- and post-RTBS serum calcium levels were also reviewed (Tables 1 and 2).

Table 1. Patient characteristics.

	Patients ($n = 33$)
Age, y	15–63
Sex	M:13–F:20
Previous radioactive iodine therapy	31
Pre-RTBS tumor-free period	6 mo–29 y (Median: 5 y)
Number of previous surgeries	
1	23
2	10
Post-RTBS follow-up period	7 mo–4 y (Median: 2 y)

Abbreviations: RTBS, Reoperative thyroid bed surgery.

All patients underwent a detailed pre-RTBS high-resolution ultrasound examination of the neck performed by our radiology service. All patients had documented evidence of suspected recurrent/persistent PTC in the central neck compartment by high-resolution neck ultrasound examination criteria. These criteria included round shape of the soft tissue mass in the thyroid bed, hypoechogenicity or hyperechogenicity of these masses compared with adjacent muscle, lack of fatty hilum of lymph nodes, punctate calcifications, or the presence of foci of cystic necrosis as well as the presence of increased vascularity on power or color Doppler. Ultrasound-guided FNA-confirmed disease in the central neck for all patients.

A unilateral or bilateral thyroid bed exploration was performed based on the FNA-confirmed location of disease as depicted on a diagram by the ultrasonography team. There was continuous RLN monitoring throughout the operation for all patients via the Medtronic Xomed NIMS-ETT system (Medtronic Xomed, Jacksonville, FL). Intra-

Table 2. Characteristics of recurrent/persistent PTC.

	Patients ($n = 33$)
Pre-RTBS serum TG	Rising [30/33 (91%)]
Pre-RTBS high-resolution ultrasound examination	Detection of lesions [33 (100%)]
Size of lesions (on high-resolution ultrasound examination)	0.5–8.3 cm (Median: 1.4 cm)
Pre-RTBS FNA	Confirmation of lesions [33 (100%)]
Final Pathology	
PTC	30
PTC, tall cell variant	3

Abbreviations: PTC, papillary thyroid cancer; RTBS, reoperative thyroid bed surgery; TG, thyroglobulin; FNA, fine-needle aspiration.

RTBS nerve stimulation was accomplished with a monopolar electrode at 0.5 milliamperes (mAMP). In addition, 27 patients had a concurrent lateral neck dissection (unilateral or bilateral), which was performed when high-resolution ultrasound examination of the lateral neck also demonstrated suspicious lymph nodes that were confirmed to be PTC by FNA.

RESULTS

The study included 33 consecutive patients who underwent RTBS for recurrent/persistent PTC.

The following algorithm was followed for all the study patients.

Detection of Recurrent/Persistent PTC. In our practice, patients with previous thyroid surgery for PTC undergo measurement of unstimulated and stimulated serum TG serum levels at least once in the first postoperative year. In 30/33 patients, recurrent/persistent PTC was suspected because of rising serum TG levels, which were interpreted along with serum TSH and serum anti-TG antibody titers by the endocrinology service at our institution. On suspicion of recurrence or persistent disease, patients were then referred for high-resolution ultrasound examination. Three patients with anti-TG antibodies had disease detected on a routine surveillance ultrasound examination. No patients had localized disease in the thyroid bed on radioactive iodine whole-body scanning.

Pre-RTBS High-Resolution Neck Ultrasound Examination. In our practice, all patients with previous thyroid surgery for PTC undergo high-resolution thyroid bed ultrasound examination every 6 months during the first 2 years in the postoperative follow-up period, and then once a year until completing 5 years. Patients with suspected PTC recurrence/persistence based on an increasing unstimulated or stimulated serum TG level are referred for high-resolution ultrasound examination as well. Patients with high-resolution ultrasound examination findings suspicious for recurrent/persistent PTC undergo ultrasound-guided FNA to confirm recurrent/persistent PTC.

All patients in this study underwent a detailed pre-RTBS high-resolution neck ultrasound examination by our radiology department. All patients had evidence of abnormal exam findings in the central neck compartment on their pre-RTBS high-resolution ultrasound examination. Those abnormalities included change in the shape, echogenicity, calcification, or necrosis of paratracheal lymph nodes or soft tissues of the central neck. FNA-confirmed PTC sites were plotted on a standard diagram of the neck along with their size and were given specific numbers to help track them during surgical intervention. The high-resolution ultrasound examination findings were compared with intra-RTBS findings and post-RTBS final histopathologic reports, and recurrent/persistent PTC in the thyroid bed was confirmed in all patients.

Operative Techniques. All patients underwent pre-RTBS documentation of vocal fold (VF) motion by fiberoptic laryngoscopy, which demonstrated the following: 29 patients had no evidence of VF motion impairment pre-RTBS; in contrast, 4 patients had VF motion impairment identified. The Medtronic Xomed NIMS-ETT system was used throughout the surgical procedure to assist with identification and preservation of the RLN. All RLNs (53/53) at risk from surgery were successfully identified in all the study patients. Three RLNs were electively resected because of tumor involvement by a large paratracheal mass or tumor densely adherent to the RLN at the cricothyroid membrane.

Outcomes. There were no reports of unexpected RLN injury or VF paralysis, permanent hypocalcemia, or other surgery-related morbidity. Two patients had transient hypocalcemia as a result of RTBS, which improved with oral calcium and vitamin D supplementation with subsequent normal serum intact parathyroid hormone levels. Thirty-one patients had an obvious decrease in post-RTBS serum TG levels, while 2 patients did not have a remarkable decrease of the serum TG levels postoperatively, because of the presence of lung metastases. All patients underwent high-resolution neck ultrasound examination upon follow-up that confirmed removal of all FNA-confirmed areas of PTC identified on the pre-RTBS examination (Table 3).

DISCUSSION

This study elucidates an RTBS algorithm for recurrent/persistent PTC that can be effectively performed with minimal morbidity. No patient in our study incurred any unexpected RLN injury, permanent hypocalcemia, or any other surgical complication. This algorithm has 3 main compo-

Table 3. Outcomes.

	Patients with RTBS ($n = 33$)
RLN	
Pre-RTBS VF motion	
Normal	29 (88%)
Abnormal	4 (12%)
Intra-RTBS RLN identification	
Identified [53/53 RLNs (100%)]	
Dissection	30 pts (50/50 RLNs)
Elective resection	3 pts (3/3 RLNs)
Post-RTBS VF motion	
Normal	26 (79%)
Abnormal (paresis or paralysis)	7 (21%)
Unexpected Op. injury	0
Hypocalcemia (serum Ca)	
No symptomatic hypocalcemia	31 (94%)
Temporary (1–6 mo; oral treatment)	2 (6%)
Permanent	0
Others	
(Hematoma, vascular, or tracheoesophageal injury)	0
Postoperative hospital stay period	1–9 d (Median: 2 d)

Abbreviations: RLN, recurrent laryngeal nerve; RTBS, reoperative thyroid bed surgery; VF, vocal fold.

nents. First patients with a rising serum TG level and negative whole-body radioactive iodine scan warrant further investigation, especially with high-resolution neck ultrasound examination. Second, high-resolution ultrasound-guided FNA of suspicious lesions within the thyroid bed and lateral neck is performed. The location and size of the lesions demonstrating PTC are carefully mapped on a standard neck diagram. Third the extent of RTBS performed should be based on high-resolution thyroid bed ultrasound examination findings and mapping of recurrent/persistent PTC.

Serum TG level measurement is the cornerstone of early detection and monitoring for thyroid cancer.[5] The practice by the endocrinology team in our institution is to perform measurement of unstimulated and stimulated TG levels at least once in the first posttreatment year to enable early detection of recurrent/persistent PTC after previous thyroid surgery. Moreover, it has been reported in the literature that the relative risk for thyroid cancer–related death significantly increases with late detection and with more local and distant metastases.[6–8]

Thyroid ultrasound is widely accepted as the first-choice, inexpensive, fast, and reliable imaging modality for evaluating thyroid-related lesions and in screening for locoregional metastasis[9]; conventional and multislice CT are inferior to ultrasound for the differential diagnosis of those lesions.[10] Moreover, thyroid ultrasound-guided FNA has been proven to be a useful diagnostic tool for thyroid lesions measuring less than 1 cm, because the percentage of its unsatisfactory results has been found to be unrelated to the size of the lesions.[11] Because thyroid ultrasound is highly operator-dependant, ultrasound studies of similar subsets of patients have to be performed by a trained sonographer.[12] The purpose of this study was not to assess the utility of high-resolution neck ultrasound in screening for PTC metastasis; however, recurrent/persistent PTC was accurately localized in all the study patients, when comparing the high-resolution neck ultrasound examination–generated neck diagram to the senior author's operative notes and the final histopathologic evaluation of these lesions.

VF examination by fiberoptic laryngoscopy was performed in all the study patients prior to RTBS to document VF motion and RLN function in previously operated patients. A previous study by our team[13] demonstrated that in some cases, VF motion impairment may be asymptomatic and may even be contralateral to the side of the FNA-confirmed PTC recurrence where surgery will be taking place. Preoperative VF examination helps in counseling patients appropriately about the risks of surgery and in outlining a plan for the extent of surgery while minimizing the medicolegal ramifications of iatrogenic RLN injury and its sequelae.[13] Some authors suggest that there is an increased risk of RLN injury in RTBS[3]; therefore, we recommend preoperative VF examination for this subset of patients and careful patient counseling outlining the sequelae that result from unilateral or bilateral VF paralysis.

Intraoperative RLN identification and dissection significantly reduces the risk of its injury and is superior to limited nerve exposure, especially in these cases.[14] The surgeon can expect to encounter difficulty in identifying and preserving the RLNs during RTBS. We found that previous surgery caused anatomical alteration in the thyroid bed and the typical landmarks used for the identification of the RLN were not readily apparent. Our finding is consistent with previous reports stating that in RTBS, the RLNs are usually encased in fibrotic tissue that distorts the anatomy of the central neck area.[15] An intraoperative nerve monitoring system has been used throughout RTBS for all patients in this study to assist with RLN identification and to

avoid unexpected injury. With the advent of multiple RLN-monitoring user-friendly systems, surgeons can easily employ this technology for all patients undergoing RTBS. A major concern about employing intraoperative nerve monitoring systems is surgeon reliance on the monitoring systems. It cannot be emphasized enough, however, that the use of the monitoring systems does not preclude the need for meticulous technique and careful surgical dissection to reduce RLN injury, especially in RTBS. All functioning RLNs for the sides being operated on in this study were successfully identified. We recommend the use of nerve-monitoring systems when attempting RTBS in this subset of patients.

There are several techniques available for intraoperative RLN monitoring. A previous study described a system using hook wire electrodes placed into the vocal folds.[15] Potential complications with this method include hematoma development and dislodgement of the electrodes. It requires placement by a physician skilled at operative direct laryngoscopy and a technician to monitor the EMG, thus this technology may not be practical for all surgeons. We used the Medtronic Xomed NIMS-ETT system for nerve monitoring, which has some advantages when compared with the system using hook wire electrodes. The Medtronic Xomed NIMS-ETT system (and other similar commercially available systems) does not directly invade the vocal folds, does not lengthen the duration of the procedure, and does not require a skilled technician to deploy the electrodes into the vocal folds or monitor the EMG. Furthermore, the surface electrode is as sensitive as intramuscular electrodes.[16] However, the disadvantages of these systems include the increased cost of the endotracheal tube (approximately $200 for each) and the possibility of endotracheal tube migration during the procedure, rendering a false negative upon stimulation of the RLN.

Some authors argue that RTBS is associated with a higher incidence of significant hypocalcemia[3,4] as well as RLN injury and that every effort should be made to avoid RTBS by performing a definitive and more radical initial treatment.[3] Frozen section evaluation and reimplantation of parathyroid tissue was utilized to help minimize long-term hypocalcemia in this patient population. We attribute the disparity between their findings and our study results to our strict adherence to the surgical algorithm described in this article. There was no evidence of tumor recurrence/persistence in the thyroid bed for all the study patients as documented by at least 1 follow-up high-resolution thyroid bed/neck ultrasound examination. Our goal in this study was to report our results when applying our algorithm. We counsel the patients that safely preventing disease progression in the central neck is our primary goal. Disease progression in this critical area can result in RLN paralysis and tracheal, laryngeal, or esophageal invasion. The patient's hyperthyroglobulinemia might not be cured, as occult regional or distant metastases that are undetectable using neck ultrasound or other state-of-the-art imaging studies may limit our ability to do so. The size of our case series is consistent with previous reports discussing RTBS.[15] Although our report has the bias of retrospective studies, the careful correlation between our surgical records and the endocrine and radiology services further strengthens our results. Our study lacks long-term post-RTBS follow-up for some patients, which may limit the evaluation of long-term disease control in the thyroid bed.

CONCLUSION

Safe and effective RTBS is based on a multidisciplinary approach that enables the identification and localization of recurrent/persistent PTC. The surgical algorithm for RTBS described provides a pathway that all endocrine-head and neck surgeons can comfortably utilize to treat this complex and challenging patient population to prevent disease progression in the central neck and its associated morbidities.

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