

Neck compartment lymph-node dissection results in clinical benefit for the majority of patients with recurrent or persistent papillary thyroid cancer but may have complications.

Schuff KG, Weber SM, Givi B, Samuels MH, Andersen PE, Cohen JI. Efficacy of nodal dissection for treatment of persistent/recurrent papillary thyroid cancer. *Laryngoscope* 2008;118:768-75.

SUMMARY

BACKGROUND Papillary thyroid cancer (PTC) has a recurrence rate of up to 30%. The current American Thyroid Association (ATA) treatment guidelines recommend lymph-node compartment-directed surgery as the first line of therapy for patients with locoregional cervical metastases and no evidence of distant metastases. However, the likelihood of such repeat surgical interventions in rendering patients free of disease is unclear. The aim of this retrospective study was to determine the efficacy and safety of central or lateral neck-lymph-node dissection in patients with recurrent PTC.

METHODS This is a retrospective chart review of patients receiving central or lateral neck compartment dissections for persistent or recurrent PTC treated from January 2004 through March 2006. Seventy-five patients underwent 79 lymph-node dissections and were evaluated for safety of the procedure. Thirty-eight dissections from the safety group were excluded from the efficacy analysis because of any of the following features: distant metastases, presence of antithyroglobulin (Tg) antibodies, postoperative radioiodine therapy prior to Tg measurement, no prior radioiodine ablation, known residual macroscopic disease, or undetectable preoperative Tg. Of the 41 remaining dissections, 30 were evaluable for cure based on preoperative and postoperative stimulated Tg measurements. Patients were considered cured if their postoperative thyrotropin (TSH)-stimulated Tg was $<2.0 \mu\text{g/L}$. The clinical status of the remaining patients was stratified according to the following postoperative Tg reductions: near-complete ($\geq 80\%$), major (50 to 79%), minor (20 to 49%), unchanged (within 20% of preoperative values), or increased ($>20\%$). Patients who had a major or near-complete response were considered to be clinically improved.

RESULTS The study population comprised 75 patients with recurrent or residual PTC who underwent selective central compartment dissection with or without lateral lymph-node compartment neck dissections performed by a single surgeon at a university hospital. All patients were previously treated with total thyroidectomy; the majority (92%) received radioactive iodine for remnant ablation. Fifty-seven patients (72%) had undergone lymph-node surgery prior to the study period.

All but seven patients (9%) had lymph-node involvement of the central or lateral neck; however, five resections revealed no lymph-node involvement and two found tumor in other sites. The central neck compartments contained tumor in 80% of resections, performed alone or in combination with lateral dissections; only 11% of patients had lateral disease in the absence of central compartment involvement. The lateral compartments were found to have malignant lymph nodes in 63% of the patients. Bilateral disease was present in 46% of the lymph-node resections.

Of the 41 resections evaluable for efficacy, 30 had paired preoperative and postoperative stimulated serum Tg levels. Of the remaining 11 resections without stimulated Tg postoperatively, nine had paired preoperative and postoperative unstimulated Tg levels to assess the benefit of surgery. The two patients without paired Tg levels were not cured based on the detectable unstimulated postoperative serum Tg value.

Sixteen of the 30 patients with postoperative stimulated Tg levels were determined to be cured (Figure 1). There was evidence of a clinical benefit, defined by a near-complete or major Tg reduction, in an additional 12 resections. The two groups combined revealed a clinical benefit or cure in 28 of 39 (72%) resections. The Tg values for each group based on the response to surgery are shown in Figures 2 and 3.

A mean of 29 lymph nodes were removed in 79 resections. Of the removed lymph nodes, an average of 7 were positive for metastatic disease; more lymph nodes were positive for malignancy among resections that were not curative as compared with those that were curative (8 vs. 6, $P = 0.02$). There also was a tendency toward bilateral disease with noncurative resections, though this was not statistically significant (14 vs 5, $P = 0.066$).

There were 25 minor complications among the 79 resections (32%), including transient hypoparathyroidism ($n = 12$, 16%), hematoma/seroma/abscess ($n = 9$, 11%), cellulitis ($n = 2$, 3%), temporary recurrent laryngeal-nerve paresis ($n = 1$, 1%), and keloid ($n = 1$, 1%). In all, there were 7 major complications (9%):

Outcome Assessment According to The Changes in Preoperative and Postoperative Thyroglobulin Levels

The Outcome Among 39 Classifiable Resections

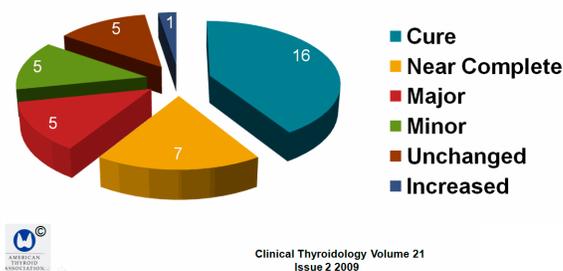


Figure 1. Outcome assessed according to thyroglobulin response to surgery. Patients were considered to be cured if postoperative TSH-stimulated Tg was $<2.0 \mu\text{g/L}$. The remaining patients were stratified by their postoperative Tg reductions as near-complete ($\geq 80\%$), major (50–79%), minor (20–49%), unchanged (within 20% of preoperative values), or increased ($>20\%$).

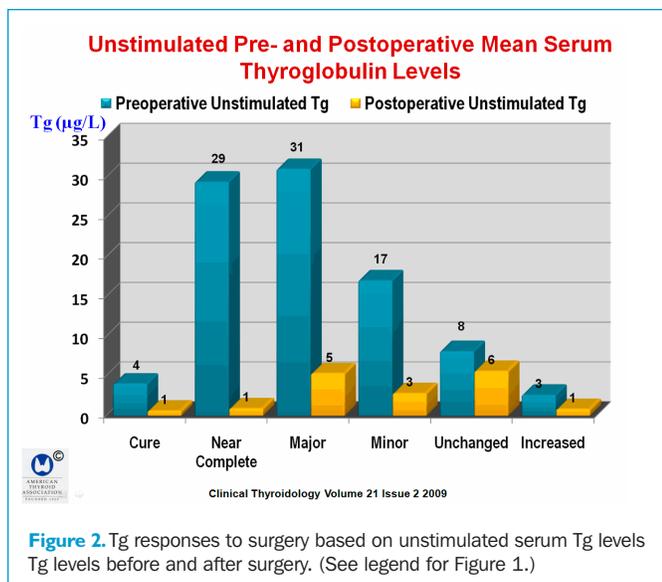


Figure 2. Tg responses to surgery based on unstimulated serum Tg levels before and after surgery. (See legend for Figure 1.)

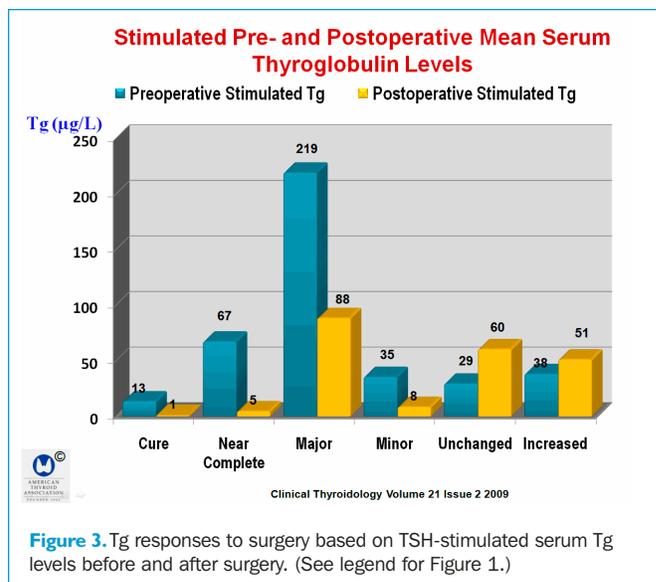


Figure 3. Tg responses to surgery based on TSH-stimulated serum Tg levels before and after surgery. (See legend for Figure 1.)

permanent hypoparathyroidism (n = 5, 7%), significant abscess requiring tracheostomy (n = 1), and deep venous thrombosis with subsequent pulmonary embolism (n = 1). There were no cases of permanent recurrent laryngeal-nerve damage.

CONCLUSION Lymph-node compartment dissection is not always a safe procedure for patients with recurrent or persistent PTC, even in the hands of an experienced surgeon, but it achieves some clinical benefit in almost 75% of patients.

COMMENTARY

The study by Schuff et al. addresses a very important question for the management of PTC: How often is repeat surgery likely to render a patient with recurrent or residual lymph-node metastases free of disease? The Schuff study found that resection of recurrent metastatic lymph nodes resulted in cure for 41% of patients and a clinical benefit in 72% of patients, as measured by a reduction in Tg of greater than 50%. An essential corollary to this issue is: How safe is the reoperation in terms of long-term morbidity? There are surprisingly little data to answer the first question when counseling a patient about reoperation for cervical lymph-node metastases. Most studies are limited by the concomitant use of radioiodine, lack of a unified definition for freedom from disease, and the retrospective nature of the studies (1-3). Current data support the findings of the Schuff study that only 20 to 40% of patients are deemed free of disease after a reoperation for recurrent or residual thyroid cancer in the form of cervical-lymph-node metastases (1-3). Likewise, the rate of postoperative complications in this patient population was in keeping with previous studies (4,5). Experience of the surgeon is a critical factor in determining the rates of postoperative hypocalcemia and vocal-cord paresis (6), and should be taken into account when counseling a patient for surgery. In the experienced hands of surgeons such as in this study, the likelihood of developing a permanent complication is low.

Patients with PTC have a high rate of lymph-node metastases at the time of initial surgery, ranging from 20 to 50% with standard pathology assessment (7), but are considerably higher when sophisticated molecular techniques are used to detect micrometastases (8). Many patients initially undergoing total thyroidectomy without central compartment dissection, with or without lateral neck compartment dissection, may present with

macroscopic tumor years after initial treatment when lymph-node metastases have grown large enough to attract clinical attention. Many such patients will be considered for reoperation to render them free of disease. However, many questions remain concerning the optimal extent of surgery in this setting. A large retrospective study (9) of patients with untreated PTC found that those with one to five central compartment lymph-node metastases had a 69% chance of ipsilateral lateral neck lymph-node involvement. Of those with more than five central compartment lymph nodes, 100% had ipsilateral involvement, and 60 to 71% also had contralateral involvement. This and other studies of prophylactic neck dissection that yield high rates of previously undetectable lymph-node metastases highlight a major issue. The American Thyroid Association (ATA) guidelines suggest systematic neck lymph-node dissection, referring to en bloc dissection of anatomic neck compartments, as compared with selectively excising lymph nodes (“berry picking”), which is not recommended. Prophylactic dissection denotes removal of lymph nodes that are considered normal preoperatively or intraoperatively, and therapeutic dissection refers to removal of malignant lymph nodes identified before or during surgery. The revised ATA guidelines suggest that prophylactic central-compartment neck dissection (unilateral or bilateral) may be performed in patients with PTC with clinically uninvolved central neck lymph nodes, especially for advanced primary tumors (T₃ or T₄) and that near-total or total thyroidectomy without prophylactic central neck dissection may be appropriate for small (T₁ or T₂) noninvasive clinically node-negative PTCs and most follicular cancers. The guidelines for lymph-node compartment dissection in patients who have previously undergone thyroidectomy are less clear, mainly because the risk for central compartment dissection is higher when patients undergo reoperation (10). Repeat surgery may result in low success rates because of the presence of large

and sometimes invasive lymph-node metastases in unexplored neck compartments.

Although studies of neck compartment dissection for recurrent or persistent disease yield high rates of positive lymph-node involvement, the long-term benefit of achieving a disease-

free status is uncertain, making it difficult to advise central compartment reoperation. Radioactive iodine therapy may be a more useful approach providing the tumor is iodine-avid and bulky metastases have been surgically excised.

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References

1. 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;25:526-31.
2. Coburn M, Teates D, Wanebo HJ. Recurrent thyroid cancer: role of surgery versus radioactive iodine (I131). *Ann Surg* 1994;219:587-95.
3. Travagli JP, Cailleux AF, Ricard M, et al. Combination of radioiodine (¹³¹I) and probe-guided surgery for persistent or recurrent thyroid carcinoma. *J Clin Endocrinol Metab* 1998;83:2675-80.
4. Kim MK, Mandel SH, Baloch Z, et al. Morbidity following central compartment reoperation for recurrent or persistent thyroid cancer. *Arch Otolaryngol Head Neck Surg* 2004;130:1214-6.
5. Henry JF, Gramatica L, Denizot A, et al. Morbidity of prophylactic lymph node dissection in the central neck area in patients with papillary thyroid carcinoma. *Langenbecks Arch Surg* 1998;383:167-9.
6. Sosa JA, Bowman HM, Tielsch JM, et al. The importance of surgeon experience for clinical and economic outcomes from thyroidectomy. *Ann Surg* 1998;228:320-30.
7. Cooper DS, Doherty GM, Haugen BR, et al. Management guidelines for patients with thyroid nodules and differentiated thyroid cancer. *Thyroid* 2006;16:109-42.
8. Arturi F, Russo D, Giuffrida D, et al. Early diagnosis by genetic analysis of differentiated thyroid cancer metastases in small lymph nodes. *J Clin Endocrinol Metab* 1997;82:1638-41.
9. Machens A, Hauptmann S, Dralle H. Lymph node dissection in the lateral neck for completion in central node-positive papillary thyroid cancer. *Surgery* 2009;145:176-81.
10. White ML, Doherty GM, Gauger PG. Evidence-based surgical management of substernal goiter. *World J Surg* 2008;31:895-904.

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