

Routine ipsilateral level VI lymphadenectomy reduces postoperative thyroglobulin levels in papillary thyroid cancer

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Background. Lymphadenectomy in clinically node-negative papillary thyroid cancer (PTC) is controversial. The aim of this study is to determine whether routine ipsilateral level VI lymphadenectomy (LNDVI) has advantages over total thyroidectomy (TT) alone.

Methods. A retrospective cohort study was performed. Patients undergoing surgery for clinically node-negative PTC >1 cm were included. Group A had TT and LNDVI. Group B had TT alone. The number of radioiodine treatments and postablative stimulated serum thyroglobulin (TG) levels were compared.

Results. From 1995 to 2005, 447 patients with clinically node-negative PTC underwent surgery. Group A (n = 56) had TT and LNDVI. Group B (n = 391) had TT alone. Tumor size was equivalent (group A, 20 mm; group B, 23 mm; P = .14) as were MACIS (metastasis, age, completeness of resection, invasion, and size) scores (group A, 4.70; confidence interval, 4.23-5.17; group B, 4.73; confidence interval, 4.4-5.05). Serum postablative TG levels were lower in group A (0.4 µg/L) compared with group B (9.3 µg/L), P = .02. More patients had undetectable TG levels in group A (72%) than in group B (43%) (P < .001). Long-term complications rates were the same.

Conclusions. In PTC the addition of routine LNDVI results in lower postablation levels of TG and higher rates of athyroglobulinemia when compared with TT alone. (Surgery 2006;140:1000-7.)

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LOCOREGIONAL LYMPH NODE METASTASIS is a common finding in papillary thyroid cancer (PTC) occurring in 20% to 50% of cases when the usual histologic techniques are employed.^{1,2} The central compartment of the neck, also known as level VI, is the region most frequently involved.^{3,4} The level VI compartment incorporates the Delphian/prelaryngeal, pretracheal, and paratracheal lymph nodes.⁵ The prelaryngeal nodes lie in the vicinity of the pyramidal lobe of the thyroid. The pretracheal and

paratracheal nodes lie anterior to the trachea and in the region of the tracheo-esophageal groove, respectively.

When lymph node metastases are clinically evident either on physical examination or sonograph, it is generally accepted that surgical excision or lymphadenectomy (LND) is the best form of treatment.⁶ The surgical approaches most frequently used in this scenario are modified radical lymph node dissection and selective node dissection.⁷ While the management of clinically apparent nodes is generally agreed upon in most centers, controversy exists regarding the role of prophylactic central LND in cases in which lymphadenopathy is not evident.^{8,9}

The potential benefits of routine LND, particularly of the level VI compartment, are a reduction in recurrent or persistent disease and avoidance of reoperative surgery in a field that places the recurrent laryngeal nerve at significant risk of injury. The disadvantage of performing LND routinely is a

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potential increase in perioperative complications rates, particularly hypoparathyroidism and recurrent laryngeal nerve dysfunction.

The aim of this study is to examine the benefits and complications of routine ipsilateral level VI lymphadenectomy (LNDVI) in patients with PTC and no clinical evidence of lymphadenopathy preoperatively.

PATIENTS AND METHODS

A retrospective cohort study of all patients undergoing surgical intervention for PTC at the University of Sydney Endocrine Unit was undertaken. Data were retrieved from prospectively maintained surgical and nuclear medicine databases.

Patient selection. Patients included in the study had histologically proven PTC measuring over 1 cm in maximum diameter. Only patients with no clinically apparent lymph node metastases were studied. Preoperative lymph node status was determined by physical examination and routine neck ultrasonography. Only patients undergoing total thyroidectomy (TT) alone or TT in combination with LNDVI were included. Patients undergoing lymph node surgery beyond level VI were excluded from the study. Patients were stratified into 2 separate groups on the basis of the extent of their surgery. Group A consisted of those patients undergoing TT and ipsilateral LNDVI. Group B included those patients undergoing TT alone. Included in group B were patients who underwent initial diagnostic hemithyroidectomy for atypical nodules and then subsequently had completion thyroidectomy for PTC.

Surgical protocols. A standardized surgical approach for the management of PTC was established within the University of Sydney Endocrine Surgical Unit in 1995. Total thyroidectomy was incorporated as the operative treatment of choice and used when possible in all patients with PTC measuring over 1 cm. A strict protocol of preoperative and postoperative laryngoscopy performed by otolaryngologists affiliated with the unit has been followed during the study period. Laryngoscopy was performed at 2 to 6 weeks postsurgery and repeated if necessary. After TT all patients were placed on calcium supplements routinely (1200 mg twice daily) with a gradual reduction over the following 3 weeks. Serum calcium levels were measured twice daily for the first 2 days and then at 2 weeks and 3 months postoperatively, or until the patient became normocalcemic without the need for calcium supplementation. Postoperative hypocalcemia was defined as a serum calcium level of less than 8 mg/dL at any point after surgery. Hypoparathyroidism was defined as the ongoing need for calcium

or vitamin D supplementation at 6 months after surgery.

In 2002 the protocol for management of patients with PTC was modified to include routine ipsilateral LNDVI in combination with TT. Lymphadenectomy was performed with the use of a standardized technique immediately after thyroidectomy. The recurrent laryngeal nerve was mobilized and skeletonized along its cervical course, avoiding the use of electrocautery in close proximity to it. Lymph node dissection was performed extending from the carotid artery laterally to the midline of the trachea medially and inferiorly to the brachiocephalic or subclavian veins. Autotransplantation of the ipsilateral inferior parathyroid gland was generally undertaken. This modification in our surgical approach has enabled us to study 2 distinct cohorts of patients who have been exposed to different surgical interventions. All procedures were performed after the provision of informed consent.

After surgery, patients underwent routine radioiodine ablation with iodine¹³¹ (¹³¹I) after thyroid hormone withdrawal for at least 4 to 6 weeks. The ablative dose given was individualized on the basis of the risk profile of the tumor being treated. In general high-risk category patients were given a greater dose. Follow-up ¹³¹I scintigraphy and possible repeat ablation was then performed 6 months later and once again after thyroid hormone withdrawal. Serum thyroglobulin (TG) levels were measured at this point. A TG assay was performed with the use of the Immulite 2000 Immunoanalyser (Diagnostic Products Corp., Los Angeles, Calif) (reference range 0.8-55 µg/L).

Outcome measures. Postoperative wound infections requiring antibiotic therapy and the number of patients requiring return to the operating room for evacuation of hematoma were recorded. Data were collected to compare the rates of temporary hypocalcemia and permanent hypoparathyroidism between the groups. The rates of recurrent laryngeal nerve dysfunction both early and permanent were compared. The number of ablative doses of radioactive iodine administered to date to each patient were recorded. Serum TG levels after withdrawal of thyroid hormone at 6 months after surgery were recorded and compared between the 2 groups. Also, TG autoantibodies were measured routinely in all patients at the time of radioiodine ablation.

Statistical analysis. Data were stored and analyzed with the use of the Stata statistical software package (College Station, Tex). Continuous data was tested with the use of an unpaired Student *t*

Table I. Patient selection criteria

1. Histologically proven PTC >1 cm
2. PTC variants included
3. No clinically apparent lymphadenopathy
4. Total thyroidectomy ± ipsilateral LNDVI

LNDVI, Level VI lymph node dissection; PTC, papillary thyroid cancer.

test. Categorical data were compared with the use of univariate analysis with a 2-tailed Fisher exact test. The alpha for significance was set at 0.05. The study population gave a power of 0.8 to detect a 20% difference in outcomes.

RESULTS

In the period December 1995 to April 2005, 594 patients underwent surgical intervention for PTC within the University of Sydney Endocrine Surgery Unit. Of these, 447 had no preoperative evidence of lymph node metastases either in the central or lateral compartments on the basis of physical examination and sonography. Fifty-six patients underwent TT in combination with ipsilateral LNDVI and were designated as group A. Three hundred ninety-one patients in group B underwent TT alone. As shown in Table II, the 2 groups were equivalent in terms of mean age, gender distribution, mean tumor diameter, and MACIS score. Group B patients had a longer median follow-up (70 months vs 24.5 months), reflecting the recent introduction of routine ipsilateral LNDVI in to the surgical protocol.

Surgical complications for the 2 groups are shown in Table III. Postoperative infections and the rate of return to the operating room for evacuation of hematoma were not significantly different between the 2 study groups. In group A, 49 (88%) of patients had the inferior parathyroid gland corresponding to LNDVI autotransplanted. The mean number of parathyroid glands autotransplanted in group A patients was significantly greater than the number in group B (1.6 vs 0.9). Group A patients had a higher rate of temporary

hypocalcemia compared with group B patients; however, at 6 months there was no difference in the rate of permanent hypoparathyroidism. The overall rate of permanent hypoparathyroidism for both groups combined was 3/447 (0.7%). The incidence of temporary and permanent recurrent laryngeal nerve dysfunction, as measured by laryngoscopy, was not significantly different between the 2 groups. The overall rate of permanent recurrent laryngeal nerve injury was 4/894 (0.4%) per nerve at risk.

The mean number of lymph nodes removed from the level VI compartment in group A patients was 5.3. Twenty-one (38%) of the 56 patients in group A had evidence of lymph node metastasis on routine hematoxylin-eosin assessment. Group B patients had an average of 0.8 (95% confidence interval, 0.2-1.3) lymph nodes removed along with the thyroidectomy specimen.

The dose range of I¹³¹ administered was 3.6 to 6.1 Gbq (97-165 millicuries). The mean dose of I¹³¹ was not different between the 2 groups. At follow-up to this point, group A and B patients had undergone an equivalent number of ablative doses of radioiodine (Table IV). The 2 groups were equivalent in terms of the incidence of TG autoantibodies. Stimulated serum TG levels measured at 6 months after the initial ablation were significantly lower in group A patients. Forty (72%) patients in group A had undetectable TG levels. This proportion was significantly greater than that found in group B (43%) $P < .001$.

At this early point in follow-up there had been 2 (3.6%) cases of locoregional recurrence in group A. Both cases were lateral recurrences (involving lymph node levels II-V), which were identified with postoperative ultrasonography. In group B, there had been 22 (5.6%) cases of locoregional recurrence requiring reoperative surgery. These included 5 (1.3%) cases involving the central compartment (level VI) only. There were 2 (0.5%) cases that involved both central and lateral compartments, and 15 (3.8%) in which only the lateral lymph node compartments were involved.

Table II. Patient characteristics

	Group A	Group B	P value
No. of patients	56	391	
Mean age (y) (95% CI)	39.1 (35-43)	42.6 (37-47)	.3
Gender distribution (M:F)	16:40	109:282	
Mean tumor size (cm) (95% CI)	2.0 (1.5-2.3)	2.3 (1.8-2.9)	.14
Mean MACIS score* (95% CI)	4.7 (4.2 to 5.1)	4.73 (4.4-5.1)	.9
Median follow-up (mo)	24.5	70	

CI, Confidence interval; MACIS, thyroid cancer prognostic scoring system abbreviated by metastasis, age, completeness of resection, invasion, and size.

Table III. Postoperative surgical complications

	Group A	Group B	P value
No. of patients	56	391	
Mean no. of parathyroid glands autotransplanted (95% CI)	1.6 (1.4-1.9)	0.9 (0.7-1.0)	<.001
Postoperative infection* (%)	1 (1.8)	5 (1.3)	.76
Postoperative hemorrhage (%)	1 (1.8)	1 (1)	.6
Temporary hypocalcemia† (%)	10 (18)	32 (8)	.02
Permanent hypoparathyroidism‡ (%)	1 (1.8)	2 (0.5)	.27
Temporary RLN dysfunction (%)	1 (1.8)	4 (1.0)	.62
Permanent RLN injury (%)	0	4 (1.0)	.45

CI, Confidence interval; RLN, recurrent laryngeal nerve.

*Wound infection requiring antibiotic therapy.

†Corrected serum calcium <8 mg/dL at any point after surgery.

‡Calcium and/or vitamin D supplements required at 6 months postoperative.

In group A, 2 patients had rising TG, which corresponded to the 2 lateral recurrences identified. In group B the 20 cases of known local recurrence all had elevated and/or increasing TG levels. Four cases had increasing TG levels related to distant metastases. There have been no disease-specific deaths in either group.

DISCUSSION

The role of routine surgery for the management of apparently normal regional lymph nodes continues to be enthusiastically debated. This is true for PTC and other surgically treated malignancies. Some groups have argued that lymph node metastasis, in general, are an indicator of prognosis rather than the determining factor of prognosis; as a result the treatment of regional lymph nodes and metastasis does not effect the outcome of cancer cases.^{10,11} It has generally been accepted in the past that lymph node status impacts on local recurrence rates rather than survival. This belief has recently been questioned, with the findings of a large population-based study showing significantly higher mortality rates for differentiated thyroid cancer involving lymph nodes.¹²

The ultimate measures of cancer surgery outcome are disease recurrence and death from disease. While it may be that prophylactic LND will not alter disease-related survival rates, it is relevant to consider some intermediate outcome variables such as influence of surgery on serum TG levels because these have a more immediate impact on patient follow-up and adjuvant care. Particularly in low-risk PTC cases for which the likelihood of death from cancer is very low, it can be argued that serum TG levels are of greater day-to-day significance to the patient and treating physician.¹³

This study suggests that routine ipsilateral LNDVI for PTC allows a more thorough clearance of thyroid tissue from the area at greatest risk of metastatic disease. The incorporation of a new surgical approach must, however, achieve an acceptably low complication rate. Our data have revealed a significantly higher rate of temporary hypocalcemia in patients undergoing LNDVI. This finding has been described by others and clearly relates to the more-extensive dissection interfering with the blood supply of the parathyroid glands, particularly the ipsilateral inferior gland.⁹ However, our long term rates of permanent hypoparathyroidism and

Table IV. Details of radioiodine ablative therapy and postoperative serum thyroglobulin levels

	Group A	Group B	P value
No. of patients	56	391	
Mean no. of RAI* treatments per patient (95% CI)	1.0 (1-1.3)	1.2 (1.0-1.3)	.51
Mean dose of I ¹³¹ per treatment† (95% CI)	5.2 (4.6-5.9)	4.8 (4.3-5.2)	.2
Patients with TG antibodies present (%)	5 (9)	43 (11)	.6
Mean serum TG level‡ (95% CI)	0.41 (0-0.9)	9.3 (6.2-12)	.02
Number of patients with serum TG undetectable at 6 months† (%)	40 (72)	168 (43)	.001

CI, Confidence interval; I¹³¹, iodine¹³¹; RAI, ablative radioiodine therapy; TG, serum thyroglobulin.

*Number of ablative doses of radioiodine administered.

†Dose of I¹³¹ in GBq.

‡Serum thyroglobulin measured after withdrawal of thyroid hormone (reference range, 0.8-55 µg/L).

recurrent laryngeal nerve injury were not significantly different between groups and were in keeping with results achieved internationally.¹⁴

We believe that careful attention to operative technique helps to limit complications related to LND. Dissection should be carried out with clear visualization of the nerve throughout its cervical course. The use of sharp dissection is preferred over electrocautery, particularly in close proximity to the recurrent laryngeal nerve. An appreciation of the location and vascularity of parathyroid glands is important, particularly of the ipsilateral inferior gland. The surgeon should have a readiness to autotransplant any compromised parathyroid tissue.

Despite normal preoperative physical examination and sonography, the incidence of lymph node metastasis in our study population was 38%. Rates similar to this and higher have been described by other groups.^{4,15} We have found the intraoperative macroscopic evaluation of the central compartment nodes to be unreliable because they can frequently be enlarged as part of a reactive process or due to an underlying thyroiditis. These factors, combined with the high rate of histologic involvement, lend weight to the case for their routine removal.

After TT and radioiodine ablation, serum TG measurement is useful in detecting persistent or recurrent disease. The highest levels of sensitivity are achieved after withdrawal of thyroid hormone or after stimulation with the use of recombinant human thyrotropin.¹⁶ This study has shown that a significantly lower level of serum TG can be achieved 6 months after surgery and radioiodine ablation when ipsilateral LNDVI is performed in combination with TT versus TT alone. The more aggressive surgical approach clears both normal thyroid tissue and metastatic thyroid cancer more effectively than TT in isolation. Thyroid rests separate from the thyroid lobe in the region of the thyrothymic ligament are identified in 20% of cervical endocrine procedures.¹⁷ It is likely that the removal of these rests in addition to involved lymph nodes, particularly in the region of the tracheoesophageal groove, allows a more thorough clearance of functioning thyroid tissue, resulting in the biochemical differences we have noted.

In many centers treating thyroid cancer, an undetectable stimulated serum TG and negative whole-body radioiodine scan have become the intermediate goals of therapy.¹⁸ It is important to acknowledge that the clinical significance of minimally detectable levels of serum TG in patients who have been treated for differentiated thyroid cancer

remains unclear. Nevertheless, our approach of routine ipsilateral LNDVI delivers more athyroglobulinemic patients to our endocrinologic and nuclear medicine colleagues. This observation has the potential to simplify follow-up and lessen the need for ongoing adjuvant treatments, namely further radioiodine ablation. Longer follow-up is needed to assess the full impact of this approach on local recurrence rates and survival.

The strengths of this study relate to the careful selection of patients such that both study groups were similar in every way, aside from the difference in operative approach. The fact that both groups had equivalent MACIS scores and tumor diameter is particularly important. It is reasonable on this basis to conclude that any observed differences in outcomes may be attributable to the variation in surgical intervention. The limitations of this study center on its nonrandomized design and relatively short follow-up period. In particular it is vulnerable to bias in the LNDVI group. This group by definition had a high likelihood of PTC, which was known to the surgeon before commencing the procedure. It may be that this knowledge in some subtle way has altered the operative approach, particularly in the region of the ligament of Berry or thyroglossal duct, and thereby altered the ultimate TG values as a result. While this is possible we believe that the standardized approach to thyroidectomy adopted in the unit makes this source of bias unlikely. On the basis of the results of this study, we continue to incorporate routine ipsilateral LNDVI into our operative approach for patients with PTC.

CONCLUSION

Total thyroidectomy performed in conjunction with ipsilateral LNDVI in patients with PTC and no apparent lymphadenopathy results in significantly lower levels of serum TG and higher rates of athyroglobulinemia.

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DISCUSSION

Dr Orlo H. Clark (San Francisco, Calif). Wonderful study, and I think probably very important for all of our patients, so I congratulate you. I just had one question. You said clinically negative nodes. What do you mean—ultrasound negative, hand negative—what do you mean by that?

Dr Mark Sywak. We included those patients who were node negative on physical examination and ultrasound. In the first half of the study period the ultrasounds were performed by a variety of different outside operators; however, more recently we changed to our own surgeon-performed ultra-

sounds. So the last few years I believe the results have been a little more reliable.

Dr Orlo H. Clark. So the nodes you found when you did your ipsilateral central neck dissection were quite small; is that right?

Dr Mark Sywak. In most cases they were quite small. The point is that nodes can be enlarged due to thyroiditis or as part of a reactive process, so size is not always a reliable predictor of metastasis.

Dr Orlo H. Clark. And if you found the lateral neck node or central neck node on the other side, they were disqualified from the study?

Dr Mark Sywak. Patients with lateral neck lymphadenopathy were excluded from the study.

Dr Ian D. Hay (Rochester, Minn). I think the topic that you are describing to this society this morning is one of the most important in this decade and will be increasingly discussed at future endocrine and surgical meetings like this. I would point out to this group that, in the current “American Thyroid Association Management Guidelines for Patients with Differentiated Thyroid Cancer,” that you can pick up from the Genzyme stand outside and published in the February 2006 issue (vol 16, no. 2) of *Thyroid*, the 27th commandment of that august body reads: “Routine central compartment (level VI) neck dissection should be considered for patients with papillary thyroid cancer,” an almost identical recommendation to the conclusion on your last slide. I find it interesting that this surgical guideline was created by 10 authors, 9 endocrinologists, and 1 member of this society. I fear that, both in Australia and North America, endocrinology is increasingly pushing for more aggression by surgeons in an attempt to, as Jim Sisson has said (*J Nucl Med* 1983;24:743) “to wipe the scintigraphic slate clean” or to create “undetectable” serum thyroglobulin (TG) levels, an aim, which Blake Cady might say, has really got nothing to do with the meaning of life or death from thyroid cancer.

Having said that, at the Mayo Clinic in the past decade, we endocrinologists have increasingly expected our surgeons to perform routine central neck dissection as part of a primary operation for papillary thyroid cancer, and I think in my time, before my retirement, I hope to demonstrate that already fairly acceptable nodal recurrence rates will be further significantly diminished by such an initial surgical approach. For sure, in this country, such initial procedures will certainly reduce the “angst” level of our poor unfortunate patients, who have been driven quite crazy by obsessive-compulsive endocrinologists striving for basal serum thyro-

globulins of less than 0.1 ng/mL, which cannot be stimulated by thousand dollar recombinant hTSH injections!

I have a question for you. I think increasingly, as an endocrinologist who has spent his career seeing thousands of patients with papillary thyroid cancer, I am increasingly disgusted by the utility of thyroglobulin as a marker of surgical success. We now recognize that at the Mayo Clinic ultrasound is now our gold-standard tool to assess the efficacy of our initial surgical treatment. Ultrasound, not serum TG, is the way by which we localize neck nodal metastasis as the site of most postoperative recurrences. My question to you is: Are you increasingly employing ultrasound postoperatively as your gold standard for assessing the anatomic success of your primary surgical procedure for patients with papillary cancer?

Dr Mark Sywak. The answer to your question is yes. Thus far the TG and the whole body scan have been the factors which have directed management. However, there is now good evidence to show that the whole body scan is relatively unreliable in detection of metastasis. In our unit we tend to rely more on the findings at ultrasound if the TG is measurable or climbing. So I agree, the key in follow-up is going to be the ultrasound. I believe as surgeons we probably should include ultrasound as part of our routine follow-up.

Dr Keith S. Heller (Long Island, NY). On your recurrence data, in addition to being statistically insignificant, the total thyroidectomy group also has significantly longer follow-up. This is another reason to be very suspicious about concluding from that data that there is a higher recurrence rate.

In the earlier series when you did not have the policy of routinely dissecting level 6, if a patient had obviously clinically positive level 6 nodes, I assume that you took them out. And in the latter group, even though your policy was to always do a level 6 dissection, some of those patients had obvious gross level 6 disease that you found at surgery, and some of them had a perfectly normal-looking level 6 nodes. Can you exclude the patients with obviously positive nodes found at surgery and only look at the ones where they were not clinically suspicious? Because that is really the question. None of us would question taking out an obviously positive node.

Dr Mark Sywak. Thank you for an excellent question. Our information doesn't really dissect out these matters. There are clearly subtle things at the time of surgery that the surgeon decides on that may alter his or her approach.

However our rationale is that if you are dealing with a disease that has a 38% chance of being there, so you have a reasonably high chance when you don't suspect it of having positive lymph nodes, I believe you should take them out. When someone comes to you with a multinodular goiter having had radiation therapy as a child, you say you need to have a total thyroidectomy based on a 40% risk of malignancy. I believe it is not unreasonable to use that same sort of thinking around those high-risk level 6 lymph nodes.

Dr Keith S. Heller. It is one thing to say we think we should do it and another thing to say we have data that prove we should do it.

Dr Christopher R. McHenry (Cleveland, Ohio). This is a well-done study and was very well presented. What really will be important is the long-term outcome data to see if routine central neck dissection has any impact on recurrence or survival. Although in your expert hands, there was no difference in long-term complications, there is a potential for increased postoperative hypoparathyroidism, especially when this is done by less-experienced surgeons. My questions are: How many of your patients underwent parathyroid autotransplantation, and what was the breakdown for the group who underwent routine central neck dissection compared to those who underwent total thyroidectomy alone? What are your recommendations for parathyroid autotransplantation?

My second question is on the technique of your central neck dissection. Do you expose the brachiocephalic vein, and, if so, have you had any intraoperative difficulties with exposure?

Finally, when you compare your two groups, can't the thyroglobulin results be explained on the basis of a more complete thyroidectomy in your second group of patients after you recognized the high levels of thyroglobulin that you were getting in patients who underwent total thyroidectomy alone prior to this study?

Dr Mark Sywak. I will answer the final question first. This is a retrospective study and as such is open to selection bias. The lymph node dissection group had their operation with the surgeon going into the operating room knowing almost certainly that they have papillary thyroid cancer, and we cannot be sure that that doesn't in some way change ones operative approach. All I can say is that total thyroidectomy in our unit is the same operation in general if you are doing it for benign disease or cancer. This is certainly a critical question which can only truly be answered prospectively.

In terms of the parathyroid transplantation, there is a higher rate of parathyroid transplantation in the lymph node dissection group. The ipsilateral inferior gland almost always requires transplantation. So on average, in the lymph node dissection group, we were transplanting 2 glands as opposed to 1 gland for a total thyroidectomy alone.

Professor Antonio Stiger-Serra (Barcelona, Spain). We all were misled by the term prophylactic. I think that is the issue. And the first speaker made a good comment. Because one third would have microscopic disease that you would treat—and then two thirds have normal nodes that you would keep prophylactically. So again I think the

analysis between therapeutic treatment and prophylactic is here. And that should be addressed. And you didn't.

I think mostly what we have seen in our experience is lateral recurrence. All our cases were presented last year in Cancun and all our cases with lateral recurrence had therapeutic central neck dissection with more than 5 nodes positive. So again the issue of prophylactic I think is still open. And I think it would be nice if we could do a group analysis to see whether normal-looking nodes should really be cleared up at the first operation.

Dr Mark Sywak. Thank you for your comments.

Invited commentary: Routine central neck lymph node dissection for thyroid carcinoma

Gerard M. Doherty, MD, *Ann Arbor, Mich*

From the University of Michigan, Ann Arbor

The advisability and utility of central neck (level 6) lymph node dissection for follicular cell-derived thyroid cancer is a controversial area. In this issue of *Surgery*, and at the American Association of Endocrine Surgeons meeting in May of 2006, Dr. Sywak et al¹ have presented some important data to address this issue.

In 2002, the authors implemented a change in their routine thyroid carcinoma operation, adding ipsilateral level 6 dissection to the previous routine of total thyroidectomy. In this report, the authors compare the 2 cohorts of patients separated by this change in practice. Patients were all treated with radioiodine ablation, and follow-up included se-

rum thyroglobulin levels. The authors have used surrogate endpoints (thyroglobulin levels at 6 months) to define the clinical outcome differences between the groups, as survival and disease-free survival would rely on infrequent events and would be biased by the different lengths of follow-up. Their results show a clear difference between the groups, with lower thyroglobulin levels (mean, 0.41 $\mu\text{g/L}$ vs 9.3 $\mu\text{g/L}$), and more patients with undetectable thyroglobulin levels (72% vs 43%) in the group who had the routine level 6 dissection. The authors also showed a slight increase in the temporary hypocalcemia frequency (18% vs 8%), but ultimately no difference in the rate of permanent hypoparathyroidism.

The utility of routine level 6 dissection hinges on 2 issues: morbidity and effectiveness. These data from Sydney show that the level 6 dissection can be added to initial total thyroidectomy with no incremental permanent morbidity. In other studies, there has been some increased morbidity of the dissection, due mainly to hypoparathyroidism. These surgeons have also shown some remarkable results regarding the effectiveness of this strategy,

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