



Published in final edited form as:

Am J Surg. 2009 March ; 197(3): 342–347. doi:10.1016/j.amjsurg.2008.09.011.

Contralateral papillary thyroid cancer: Does size matter?

Susan C. Pitt, M.D., Rebecca S. Sippel, M.D., and Herbert Chen, M.D., F.A.C.S

Section of Endocrine Surgery, Department of Surgery, University of Wisconsin, Madison, WI

Abstract

Background—The optimal extent of thyroidectomy for papillary thyroid cancers (PTCs) < 1 cm is controversial. Our aim was to identify the rate and factors predictive of contralateral PTC in these patients.

Methods—We examined 228 patients with PTC who underwent either completion or total thyroidectomy and analyzed the predictive value of tumor size, histology, margin status, capsular invasion, extrathyroid extension, multifocality, and node metastases.

Results—We observed no differences in the rate of contralateral disease in patients with primary PTC \geq 1 cm compared to those < 1 cm, 30% vs. 24% respectively ($P=0.43$). Multifocality was the only factor predictive of contralateral PTC in patients with tumors < 1 cm ($P=0.02$). Patients with tumors < 0.5 cm also had a comparable rate of contralateral disease (27%).

Conclusion—The presence of contralateral PTC appears to be unrelated to the size of the primary tumor. Furthermore, in patients with PTCs < 1 cm, multifocality is a risk factor for PTC in the contralateral lobe.

Keywords

Papillary thyroid cancer; Contralateral; Size; Risk factors; Microcarcinoma

Papillary thyroid cancer (PTC) is the most prevalent histologic subtype of thyroid cancer accounting for more than 80% of all cases [1]. Fortunately, the prognosis for patients diagnosed with PTC is very favorable with a 10-year survival rate of 97% [1]. In 2008, over 37,000 adults are projected to be diagnosed with thyroid cancer in the United States, and almost 1,600 people will die from the disease [2]. Several recent reports indicate that the incidence of PTC is increasing worldwide [1–9]. This increased incidence is largely due to improved detection of papillary microcarcinomas (PMCs), defined by the World Health Organization as tumors measuring less than or equal to 1 cm in greatest dimension [1,10]. Forty-nine percent of the 2.9-fold increase in PTC incidence observed between 1973 and 2002 was due to PMCs, while an additional 38% consisted of cancers measuring between 1.1 and 2.0 cms [1]. Whether or not this increase in PTC incidence is a true epidemic or the result of enhanced detection of subclinical disease is unclear. Nonetheless, approximately 45% of the 37,000 patients diagnosed with PTC in 2008 will have tumors measuring 1 cm or smaller [1].

The management of PMCs which are often asymptomatic and undetectable by palpation has become a controversial topic. While some clinicians believe that observation is appropriate,

Corresponding Author: Susan C. Pitt, MD, 600 Highland Avenue, Clinical Science Center K4/623, Madison, WI 53792-3284, Email: E-mail: pitt@surgery.wisc.edu, Phone: 608-265-3749, Fax: 608-263-7652.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

others support surgical resection, but the optimal extent of thyroidectomy is unknown. Currently, over 70% of patients with PMCs are undergoing total thyroidectomy (TT) which is not surprising considering the rising overall number of TTs being performed each year [1,3, 11]. However, many patients are treated initially by thyroid lobectomy. In these patients with PMCs treated by lobectomy, most clinicians would argue for completion thyroidectomy (CT) if the risk of PTC in the contralateral lobe was substantial. In this study, we sought to define the rate and identify factors predictive of PTC in the contralateral lobe of patients with PMCs.

Methods

We reviewed the prospective University of Wisconsin Endocrine Surgery database to identify all patients with PTC who underwent either TT or CT from May 1994 to January 2007. Patients who did not have information on the size of their primary tumor were excluded. The following data were retrospectively reviewed and analyzed: patient demographics, extent of surgery, recurrence, tumor pathology, and histologic parameters including tumor size, follicular variant, multifocality, capsular invasion, vascular invasion, extrathyroidal extension, margin and lymph node status. Multifocal disease was defined as more than one tumor focus in the ipsilateral lobe of the primary tumor. Patients were divided into two groups based on the size of the primary tumor, ≥ 1 cm and < 1 cm for analysis. Tumors < 1 cm were further subdivided into tumors ≥ 0.5 cm and < 0.5 cm for additional examination. Approval for this study was obtained from the University of Wisconsin Human Subjects Institutional Review Board.

Data were recorded as mean \pm SD. Statistical analysis of the differences between groups was performed using unpaired t-tests for age and primary tumor size. All other analyses were carried out with two-tailed Fisher's exact tests. A *P* value of < 0.05 was considered statistically significant.

Results

We identified 243 patients with PTC who were treated by TT or CT at the University of Wisconsin. Of these 243 patients, 228 (94%) had available information on the size of their primary tumor and were included in this investigation. The average age at diagnosis of the entire cohort was 45 years, and the majority, 170 (75%), were female (Table 1). The proportion of patients with follicular variants of PTC was 15% (35 of 228). In addition, one-quarter of all patients (57 of 228) had cervical lymph node metastases at the time of initial surgery. The rate of PTC in the contralateral lobe was 29% for the entire cohort (Table 1).

Patients were initially analyzed in two groups: ≥ 1 cm and < 1 cm. One hundred fifty-eight patients (69%) had tumors ≥ 1 cm, while 70 patients (31%) had tumors less than 1 cm (Table 1). No significant differences existed between the two groups in terms of age or gender (Table 1). The average size of the primary tumors for the ≥ 1 and < 1 cm groups were 2.3 and 0.5 cms, respectively ($P < 0.0001$, Table 1). Thirteen patients in each group underwent a CT with the majority of patients treated by TT (Table 1). PTC was present in the contralateral thyroid lobe of 48 (30%) patients with primary tumors ≥ 1 cm and 18 (26%) patients with tumors measuring < 1 cm ($P = \text{NS}$). Comparison of the primary tumor histology revealed that patients with tumors ≥ 1 cm were more likely to have a positive resection margin and extension of the tumor outside of the thyroid (Table 2). The incidence of follicular variant, multifocal disease, capsular and vascular invasion, lymph node positivity, and recurrence were similar between patients with PTC ≥ 1 cm and < 1 cm (Table 2).

Evaluation of the 70 patients with primary tumors < 1 cm revealed that patients with multifocal disease in the ipsilateral lobe were significantly more likely to have contralateral tumors ($P = 0.02$, Table 3). Six of the 17 patients (35%) with contralateral PTC had multifocal disease

with more than one tumor nodule in the contralateral lobe. Furthermore, patients with a follicular variant trended toward having an increased incidence of contralateral disease, but this finding was not significant ($P=0.09$). Because no patients with tumors < 1 cm had a positive margins, we examined a resection margin of < 1 mm as an additional factor. We did not find any correlation between the presence of contralateral PTC and capsular or vascular invasion, extrathyroid extension, margin status, lymph node positivity, or recurrence. The size of the primary tumor and the presence of additional benign nodules in either lobe also were not predictive of PTC in the contralateral lobe. The average size of the contralateral tumors was 2 mm in these patients. Of note, 29% of patients with < 1 cm tumors and contralateral disease had positive lymph nodes.

Patients with tumors < 1 cm were subdivided into two additional groups based on the size of their primary tumors: ≥ 0.5 (n=40) and < 0.5 cm (n=30). This sub-division again revealed no difference in the rate of contralateral PTC. The proportion of patients with tumors ≥ 0.5 and < 0.5 cms who had PTC in the contralateral lobe was 25% (10 of 40) and 27% (8 of 30), respectively, ($P=NS$). In addition, for tumors < 0.5 cm, we analyzed the same factors listed in Table 3 for an association with contralateral PTC. In this analysis, multifocal disease again correlated with the presence of contralateral PTC ($P=0.03$). Factors not associated with PTC in the contralateral lobe of patients with tumors < 0.5 cm included a margin < 1 mm, capsular or vascular invasion, extrathyroid extension, and lymph node positivity (data not shown).

Discussion

The optimal extent of surgical resection for papillary thyroid cancer (PTC) remains a topic of debate. While consensus guidelines recommend total thyroidectomy (TT) for PTCs ≥ 1 cm, the treatment of papillary microcarcinomas (PMCs) is still controversial [12]. Furthermore, the role of completion thyroidectomy (CT) for tumors < 1 cm is undefined. In this study, we examined a cohort of 228 patients who underwent TT or CT at the University of Wisconsin from May 1994 to January 2007. We report a similar rate of contralateral PTC for patients with primary tumors ≥ 1 cm, < 1 cm, and < 0.5 cm (30%, 26%, and 27%, respectively, $P=NS$ for all) (Table 2). In patients with tumors < 1 cm and < 0.5 cm, multifocal disease was predictive of PTC in the contralateral lobe ($P=0.02$ and 0.03 , respectively).

The true incidence of contralateral PTC is difficult to estimate because around 17 percent of patients are treated by lobectomy alone [11]. Nevertheless, reported rates of contralateral PTC discovered in CT or TT specimens ranges from 13 to 56 percent [13–14]. For PMCs, up to 28 percent of patients have been reported to have PTC in the contralateral lobe at the time of histological review [13,15]. Our series is consistent with these previous reports. Twenty-nine percent (n=48) of all patients and 26% (18 of 70) of patients with primary tumors < 1 cm had contralateral PTC. Interestingly, patients with primary tumors < 0.5 cm had a similar rate of contralateral disease (27%). These data suggest that the rate of contralateral PTC is independent of primary tumor size. In a review of 150 patients who underwent CT, Grigby et al. also found that the size of the primary tumor did not predict the presence of contralateral disease [16].

While primary tumor size does not correlate with PTC in the contralateral lobe, multiple factors have been shown to predict contralateral disease. Researchers have attempted to detect such connections in order to better identify which patients would benefit from CT when PTC is discovered incidentally after lobectomy. In CT specimens, positive lymph node metastases at the initial operation and a longer time interval between lobectomy and CT have been associated with PTC in remaining lobe [17,18]. In addition, infiltration of the thyroid capsule, “tall-cell” variant, and the presence of a tumor capsule have been linked to bilateral PTC [18]. An increased incidence of contralateral PTC also has been observed in patients with a history of head and neck irradiation, but these results were not statistically significant [19]. Another

variable shown to be predictive of PTC in the contralateral lobe is ipsilateral multifocal disease [14,20]; however, these studies looked at all sizes of primary tumors.

In patients with primary tumors < 1 cm, we report that multifocal disease is a significant risk factor for contralateral tumors (Table 3). Furthermore, even in patients with primary tumors < 0.5 cm, multifocal disease remained predictive of contralateral PTC. In the literature, the rate of multifocality in PMCs ranges from 15 to 43% [21–22]. Our data are comparable in that 20 of 70 patients (29%) with tumors < 1 cm had multifocal disease. These relatively high rates of multifocal disease and contralateral PTC have led some surgeons to argue for TT or CT even in patients with PMCs [15,16,18,21]. Moreover, research on multifocal PTC has recently shown that these tumors arise from independent clonal origins of distinct tumor foci [23]. This finding strengthens the argument for performing TT or CT for tumors < 1 cm.

Despite these data, the optimal treatment for PMCs remains controversial. From 1985 to 1998, 70% of patients with PTCs < 1cm underwent TT [11]. In addition, the number of partial thyroidectomies performed annually has decreased while TTs have increased [3]. Investigations of the rate of complications after lobectomy compared to TT have reported a higher incidence of permanent recurrent laryngeal nerve injury (up to 7%) and permanent hypoparathyroidism (up to 20%) with TT [24]. Consequently, patients with PMCs are frequently treated by lobectomy to avoid this increased risk, but are subjected to a potential second operation. Furthermore, lobectomies are often performed to prevent the need for life-long thyroid hormone replacement even though nearly 50% of these patients may require hormone therapy anyway [25]. However, other investigators have discovered no differences in the rates of recurrent laryngeal nerve injury or hypoparathyroidism after lobectomy or TT [25]. Moreover, recent studies examining CT and TT report similar complication rates after these operations as well. In one study of 350 patients who underwent either CT or TT, the rates of permanent recurrent laryngeal nerve injury and permanent hypoparathyroidism were 0% and 3%, respectively [26].

Regardless of the initial surgical treatment for patients with PMCs, research has revealed that these often microscopic tumors are not benign. Rates of extrathyroid extension, capsule invasion, lymph node metastases, and distant metastases at presentation in patients with PMCs have been as great as 21%, 20%, 26%, and 3%, respectively [15,27–28]. Furthermore, as many as 7% of patients with tumors \leq 1 cm experience locoregional recurrence, 5% lymph node recurrence, and 1% mortality [15,21]. Not surprisingly, in patients with PTC, the size of the primary tumor has been shown to be unrelated to lymph node or distant recurrence [27,29]. Moreover, we and others have confirmed that tumor size also is not predictive of contralateral PTC [16]. A study by Grigbsy et al. with a mean tumor size of 2.4 cm exhibited that patients with contralateral disease have similar rates of recurrence and mortality compared to patients with unilateral disease when treated by CT with radioiodine ablation (RAI) [16]. Meanwhile, a review of 52,173 patients from the National Cancer Data Base demonstrated that the extent of surgical resection did not effect recurrence or survival in patients with PTCs <1 cm suggesting that lobectomy alone is sufficient treatment for PMCs [11].

Like any surgical decision, the selected treatment for PMCs also should take into consideration the patients' needs and any extraneous factors. In one study, when given the choice of surgery versus watchful waiting, 75% of patients with PMCs elected for surgery [30]. Over the following 5 years, the majority of patients who initially declined resection eventually selected surgery [30]. When faced with a diagnosis of cancer, even PTC which overall has a 97% 10-year survival rate, these data established that patients want their cancers removed. An individualized decision taking into account current guidelines, risk assessment, and all available patient, histologic, and other parameters should be made between the provider and the patient.

In this study, we show that the rates of papillary thyroid carcinoma (PTC) in the contralateral thyroid lobe of patients with tumors ≥ 1 cm are similar when compared to tumors < 1 cm. Furthermore, in patients with small tumors < 1 cm, multifocal disease is a significant risk factor for PTC in the contralateral lobe. These results remain valid even for patients with tumors < 0.5 cm. Our analysis is limited by a relatively small sample size, an inability to eliminate potentially confounding variables, and the inherent bias of a retrospective design despite utilization of a prospectively collected database. The consensus guidelines clearly recommend total thyroidectomy (TT) for patients with PTC ≥ 1 cm, tumor nodules in the contralateral lobe, regional or distant metastases, a history of head or neck radiation, or a family history of differentiated thyroid cancer [12]. However, our data show that the risk of tumor nodules in the contralateral lobe is the same for all sized tumors, and higher in patients with multifocal ipsilateral disease. Therefore, consideration for total or completion thyroidectomy (CT) should be made even in patients with tumors < 1 cm when significant risk of contralateral or multifocal PTC is present.

Discussion

DR. STEVEN A. DeJONG (Maywood, Illinois): Treatment of small papillary thyroid cancers still remains controversial, as the authors acknowledged in their presentation. Because of the incidence of these in autopsy series, and because of the difficulty studying the impact of small cancers on survival, I suspect that that mystery is going to be with us for some time. I think the authors did give us some important information. This is occurring at a time when there has been a clear paradigm shift in treatment. We seem to be more aggressive with these papillary thyroid cancers, advising total thyroidectomy for most all patients. Central cervical lymph node dissections now are becoming quite prevalent, along with postoperative radioactive iodine ablation. The goal is to get patients to the stage where they're not only thyroglobulin negative, but also ultrasound negative on their follow-up. I think there two points in the study that are important to emphasize: tumors less than a centimeter seem to behave similarly; and, even tiny papillary cancers seem to have the potential for lymph node metastases in the central neck.

I have a couple of questions. Number one, have your data affected your advice to patients regarding the size of thyroid nodules to be sampled with ultrasound-guided fine needle biopsies? Second, there seems to be a great number of total thyroidectomies in your series. There were only 13 completion thyroidectomies in each group that you presented. Did all these patients come with contralateral disease indicating they ought to have a total thyroidectomy or did these patients have positive fine needle biopsy for papillary cancer in their preoperative evaluation? Third, in order to know whether or not completion thyroidectomy ought to be done, we need to know how safely it can be done. So, can you comment on the morbidity and mortality rates in your institution? And my final question involves age, because oftentimes we see these patients that have had a lobectomy coming from somewhere else. It's unclear how we would manage, for example, a 65-year-old patient with a solitary incidental 5 millimeter papillary cancer found on lobectomy for a benign 4 centimeter thyroid module. Given your data, would you advise completion thyroidectomy in that patient? So, give us a little bit of insight into age. Was that a factor at all in your analysis?

DR. PITT: First, we have not changed our advice to patients. We recommend biopsy of nodules that are greater than or equal to 1 centimeter, that appear suspicious on ultrasound, or that appear to have changed in size over a time period of observation.

For the percentage of patients in our study who underwent total thyroidectomy, this is falsely elevated because we excluded those patients who underwent only a lobectomy. One thing to note is that the national average of patients who are undergoing total thyroidectomy for tumors less than 1 centimeter is approximately 70 to 80 percent at this time.

In our series, age did not appear to be a factor in the incidence of papillary thyroid cancer in the contralateral lobe. So, if we had a 65 year old patient who had an incidental 5 millimeter papillary thyroid cancer in the ipsilateral lobe of a benign finding, I think that we would still consider lobectomy as a sufficient operation.

And, lastly, for patients undergoing completion thyroidectomy, the risk of recurrent laryngeal nerve injury or hypoparathyroidism was less than 2 percent, approaching that for lobectomy alone.

DR. RICHARD A. PRINZ (Chicago, Illinois): Often it is easier to do a completion thyroidectomy when the patient has been referred to you after someone else did the original operation. So I wonder who did the original operations, and have you gone back on any of your own patients with those small microcancers, especially if there's only a single micropapillary thyroid cancer present?

DR. PITT: The patients in our study were operated on by at least four different surgeons. A certain number of the patients that were referred to us from outside institutions were actually excluded because we could not get final pathology reports on them, so we did not have size information on their primary tumors. For patients that we're currently operating on for benign disease who undergo a lobectomy and have a single microscopic focus of papillary thyroid cancer in that lobe, we are not going back and doing completion thyroidectomies for a single focus of disease.

Acknowledgements

This work was supported by the American College of Surgeons Resident Research Scholarship and NIH Grant T32 CA009614 Physician Scientist Training in Cancer Medicine.

References

1. Davies L, Welch HG. Increasing incidence of thyroid cancer in the United States, 1973–2002. *JAMA* 2006;295:2164–2167. [PubMed: 16684987]
2. American Cancer Society. Cancer Facts and Figures 2008. [Accessed July 1, 2008]. Available at: www.cancer.org/downloads/STT/2008CAFFfinalsecured.pdf
3. Mitchell I, Livingston EH, Chang AY, et al. Trends in thyroid cancer demographics and surgical therapy in the United States. *Surgery* 2007;142:823–828. [PubMed: 18063063]
4. Hodgson NC, Button J, Solorzano CC. Thyroid cancer: is the incidence still increasing? *Ann Surg Onc* 2004;11:1093–1097.
5. Smailyte G, Miseikyte-Kaubriene E, Kurtinaitis J. Increasing thyroid cancer incidence in Lithuania in 1978–2003. *BMC Cancer* 2006;6:284. [PubMed: 17156468]
6. Scheiden R, Keitpes M, Bock C, et al. Thyroid cancer in Luxembourg: a national population-based data report (1983–1999). *BMC Cancer* 2006;6:102. [PubMed: 16635261]
7. Reynolds RM, Weir J, Stockton DL, et al. Changing trends in incidence and mortality of thyroid cancer in Scotland. *Clin Endocrinol (Oxf)* 2005;62:156–162.
8. Leenhardt L, Grosclaude P, Cherie-Challine L. Increased incidence of thyroid carcinoma in France: a true epidemic or thyroid nodule management effects? Report from the French Thyroid Cancer Committee. *Thyroid* 2004;14:1056–1060. [PubMed: 15650358]
9. Liu S, Semenciw R, Ugnat AM, Mao Y. Increasing thyroid cancer incidence in Canada, 1970–1996: time trends and age-period-cohort effects. *Br J Cancer* 2001;85:1335–1339. [PubMed: 11720471]
10. Llyod, R.; DeLellis, R.; Heitz, P.; Eng, C. World Health Organization Classification of Tumours: Pathology and Genetics of Tumours of the Endocrine Organs. Lyon, France: IARC Press; 2004.
11. Billmoria KY, Bentrem DJ, Ko CY, et al. Extent of surgery affects survival for papillary thyroid cancer. *Ann Surg* 2007;246:375–384. [PubMed: 17717441]

12. Cooper DS, Doherty GM, Haugen BR, et al. Management guidelines for patients with thyroid nodules and differentiated thyroid cancer. *Thyroid* 2006;16:109–141. [PubMed: 16420177]
13. Schönberger J, Marienhagen J, Agha A, et al. Papillary microcarcinoma and papillary cancer of the thyroid < or = 1cm: modified definition of the WHO and the therapeutic dilemma. *Nuklearmedizin* 2007;46:115–120. [PubMed: 17690788]
14. Pasiaka JL, Thompson NW, McLeod MK, et al. The incidence of bilateral well-differentiated thyroid cancer found at completion thyroidectomy. *World J Surg* 1992;16:711–7116. [PubMed: 1413840]
15. Chow S, Law SCK, Chan JKC, et al. Papillary microcarcinoma of the thyroid—prognostic significance of lymph node metastasis and multifocality. *Cancer* 2003;98:31–40. [PubMed: 12833452]
16. 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;140:1043–1047. [PubMed: 17188155]
17. Pacini F, Elisei R, Capezzone M, et al. Contralateral papillary thyroid cancer is frequent at completion thyroidectomy with no difference in low- and high-risk patients. *Thyroid* 2001;11:877–881. [PubMed: 11575858]
18. Miccoli P, Minuto MN, Ugolini C, et al. Intrathyroidal differentiated thyroid carcinoma: tumor size-based surgical concepts. *World J Surg* 2007;31:888–894. [PubMed: 17426903]
19. Kawura M, Pathak I, Gullane PJ, et al. Multicentricity in papillary thyroid carcinoma: analysis of predictive factors. *J Otolaryngol* 2001;30:102–105. [PubMed: 11770951]
20. Kim ES, Kim TY, Koh JM, et al. Completion thyroidectomy in patients with thyroid cancer who initially underwent unilateral operation. *Clin Endocrinol* 2004;61:145–148.
21. Küçük NO, Tari P, Tokmak E, Aras G. Treatment for microcarcinoma of the thyroid—clinical experience. *Clin Nucl Med* 2007;32:279–281. [PubMed: 17413573]
22. Ito Y, Uruno T, Nakano K, et al. An observation trial without surgical treatment in patients with papillary microcarcinoma of the thyroid. *Thyroid* 2003;13:381–387. [PubMed: 12804106]
23. Shattuck TM, Westra WH, Ladenson PW, Arnold A. Independent clonal origins of distinct tumor foci in multifocal papillary thyroid cancer. *N Eng J Med* 2005;352:2406–2412.
24. Osmólski A, Frenkiel Z, Osmólski R. Complications in surgical treatment of thyroid diseases. *Otolaryngol Pol* 2006;60:165–170. [PubMed: 16903331]
25. Farkas EA, King TA, Bolton JS, Fuhrman GM. A comparison of total thyroidectomy and lobectomy in the treatment of dominant thyroid nodules. *Am Surg* 2002;68:678–682. [PubMed: 12206601]
26. Rafferty MA, Goldstein DP, Rotstein L, et al. Completion thyroidectomy versus total thyroidectomy: Is there a difference in complication rates? An analysis of 350 patients. *J Am Coll Surg* 2007;205:602–607. [PubMed: 17903736]
27. Pellegriti G, Scollo C, Lumera G, et al. Clinical behavior and outcome of papillary thyroid cancers smaller than 1.5 cm in diameter: study of 299 cases. *J Clin Endocrinol Metab* 2004;89:3713–3720. [PubMed: 15292295]
28. Nam-Goong IS, Kim HY, Gong G, et al. Ultrasound-guided fine-needle aspiration of thyroid incidentaloma: correlation with pathological findings. *Clin Endocrinol (Oxf)* 2004;60:21–28.
29. Cheema Y, Repplinger D, Elson D, Chen H. Is tumor size the best predictor of outcome for papillary thyroid cancer? *Ann Surg Oncol* 2006;13:1524–1528.
30. Ito Y, Uruno T, Nakano K, et al. An observational trial without surgical treatment in patients with papillary microcarcinoma of the thyroid. *Thyroid* 2003;13:381–387. [PubMed: 12804106]

Table 1

Patient Demographics and Characteristics

	Total	Primary tumor \geq 1 cm	Primary tumor < 1 cm	<i>P</i> value
Number (%)	228	158 (69)	70 (31)	----
Gender, Female (%)	170 (75)	114 (72)	56 (80)	NS
Mean age \pm SD	45 \pm 16	45 \pm 17	45 \pm 15	NS
Age range (y)	8 – 88	8 – 88	15 – 79	NS
Avg. tumor size \pm SD (cm)	1.7 \pm 1.0	2.3 \pm 1.3	0.5 \pm 0.3	0.0001
Total thyroidectomy (%)	202 (89)	145 (92)	57 (81)	NS
PTC in contralateral lobe (%)	65 (29)	48 (30)	18 (26)	NS

PTC=Papillary thyroid cancer

Table 2

Pathologic Features by Tumor Size

	Primary tumor \geq 1 cm (n=158)	Primary tumor < 1 cm (n=70)	<i>P</i> value
Follicular variant (%)	32 (20)	14 (20)	NS
Multifocal (%)	32 (20)	20 (29)	NS
Tumor capsule invasion (%)	11 (7)	5 (7)	NS
Vascular invasion (%)	1 (0.6)	1 (1.4)	NS
Extrathyroid extension (%)	31 (20)	6 (9)	0.05
Positive Margin (%)	14 (24)	0 (0)	<0.01
Positive lymph node (%)	43 (27)	14 (20)	NS
Lymph node recurrence (%)	11 (6.9)	1 (1.4)	NS

Table 3
Tumor Histology and Predictors of Contralateral PTC for Tumors < 1 cm

	Positive Contralateral lobe (n=17)	Negative Contralateral lobe (n=53)	<i>P</i> value
Follicular variant (%)	6 (35)	8 (15)	0.09
Multifocal (%)	9 (53)	11 (21)	<0.02
Tumor capsule invasion (%)	1 (5.9)	4 (7.5)	NS
Vascular invasion (%)	0 (0)	1 (1.9)	NS
Extrathyroid extension (%)	1 (5.9)	5 (9.4)	NS
Margin < 1mm (%)	2 (12)	6 (11)	NS
Positive lymph node (%)	5 (29)	9 (17)	NS
Lymph node recurrence (%)	0 (0)	1 (1.9)	NS

PTC=Papillary thyroid cancer