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A Randomized Controlled Clinical Trial: No Clear Benefit to Prophylactic Central Neck Dissection in Patients with Clinically Node Negative Papillary Thyroid Cancer

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Abstract

Objective: The aim of this prospective randomized-controlled trial was to evaluate the risks/benefits of prophylactic central neck dissection (pCND) in patients with clinically node negative (cN0) papillary thyroid cancer (PTC).

Background: Microscopic lymph node involvement in patients with PTC is common, but the optimal management is unclear.

Methods: 60 patients with cN0 PTC were randomized to a Total Thyroidectomy (TT) or a TT+pCND. All patients received postoperative laryngoscopies and standardized radioiodine treatment. Thyroglobulin (Tg) levels and/or neck ultrasounds (US) were performed at 6 weeks, 6 months and 1 year.

Results: Tumors averaged 2.2 ± 0.2 cm and 11.9% had extra-thyroidal extension. 30 patients underwent a pCND and 27.6% had positive nodes (all ≤ 6 mm). Rates of post-operative PTH <10 (33.3% vs. 24.1%, $p=0.57$) and transient nerve dysfunction (13.3% vs. 10.3%, $p=1.00$) were not significantly different between groups. Six weeks after surgery, both TT and TT+pCND were

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equally likely to achieve a $Tg < 0.2$ (54.5% vs. 66.7%, $p=0.54$) and/or a stimulated Tg (sTg) < 1 (59.3% vs. 64.0%, $p=0.78$). At 1 year, rates of $Tg < 0.2$ (88.9% vs. 90.0%, $p=1.00$) and sTg < 1 (93.8% vs. 92.3%, $p=1.00$) remained similar between groups. Neck US at 1 year were equally likely to be read as normal (85.7% in TT vs. 85.1% in pCND, $p=1.00$).

Conclusions: cN0 PTC patients treated either with TT or TT+pCND had similar complication rates after surgery. While microscopic nodes were discovered in 27.6% of pCND patients, oncologic outcomes were comparable at 1 year.

MINI ABSTRACT

Patients with papillary thyroid cancer treated either with total thyroidectomy or a total thyroidectomy plus a prophylactic central neck dissection had similar complication rates after surgery. While microscopic nodes were discovered in 27.6% of patients undergoing a central neck dissection, oncologic outcomes were comparable at 1 year.

INTRODUCTION

Thyroidectomy is the standard treatment for papillary thyroid cancer (PTC). When macroscopic nodal disease is present (i.e. visualized on imaging pre-operatively or identified intra-operatively), surgical resection is the best management [1–3]. However, the management of microscopic lymph node, which is present in 20–80% of patients, is unclear [4–8]. Survival with PTC is excellent, but recurrence remains a frequent challenge. Since microscopic nodal disease is often not evident on pre-operative imaging, the 2006 American Thyroid Association (ATA) Guidelines for the treatment of thyroid nodules and cancer stated a “*prophylactic central neck dissection should be considered in all patients with PTC*”[9].

Publication of this guideline triggered a debate within the endocrine community. While microscopic nodal disease is found when a prophylactic neck dissection is performed, it is unclear if removing this microscopic disease impacted the long-term prognosis or decreased the risk of recurrence [10–12]. Since a central neck dissection requires a more extensive manipulation of the recurrent laryngeal nerve and parathyroid glands, this additional dissection was thought to increase the risks of surgery. In the absence of a significant benefit, it was unclear if exposing patients to the potential additional surgical risks of a prophylactic CND (pCND) was appropriate [13].

The aim of this prospective randomized-controlled trial (RCT) was to evaluate the risks/benefits of a pCND in patients with clinically node negative PTC. Since it may take 10–20 years to identify some clinical recurrences [14], we focused on the short-term predictors of disease recurrence including unstimulated Thyroglobulin (Tg) and stimulated Tg (sTg) levels. To assess the risks of surgery, patients received comprehensive laboratory and diagnostic testing, but were also given validated quality of life questionnaires to evaluate the impact on the patient’s quality of life (QOL).

METHODS

Eligibility

Recruitment for this single institution study opened in June of 2014. All patients with a confirmed diagnosis of PTC or a fine needle aspirate (FNA) and/or ultrasound (US) that were suspicious for PTC were considered for enrollment. Patients were eligible if they were between the ages of 21–70, had no other malignancy, and had no evidence of nodal disease or distant metastasis at their initial presentation. The University of Wisconsin–Madison Health Sciences Institutional Review Board approved this study, and all participants provided written informed consent before enrollment. The study enrollment is highlighted in the CONSORT diagram (FIGURE 1).

To be eligible for randomization, patients were required to have a proven diagnosis of PTC ≥ 1 cm. If the preoperative FNA was not diagnostic, a frozen section was performed in the operating room (OR) to confirm the diagnosis. All patients underwent a preoperative cervical US that was read by a dedicated radiologist with expertise in US. If the US was read as “no evidence of nodal disease” the patient was eligible for the study, but randomization did not occur until after an assessment of the central neck nodes was performed in the OR by the operating surgeon. If the surgeon felt that there was intraoperative evidence of nodal pathology and a CND was clinically indicated, then the patient was not randomized.

Randomization

After confirmation of a diagnosis of PTC and an intraoperative assessment confirming no evidence of nodal disease, 61 patients with PTC were randomized to a Total Thyroidectomy (TT) or a TT+pCND. Randomizations were assigned using a block randomization scheme, stratified by age and tumor size. A sealed envelope was given to the surgeon prior to surgery and was opened in the OR by the nurse, once the total thyroidectomy was complete and the patient was confirmed to be eligible for randomization. If randomized to pCND, a comprehensive unilateral CND was performed following the technique outlined in the ATA Consensus Statement [15]. If there was a suspicion for a bilateral tumor, the pCND was done on the side of the largest biopsy proven tumor. After completion of the CND, the adequacy of the dissection was confirmed by another study surgeon in the OR or by the study PI remotely by reviewing a photograph of the resection bed. All surgeries were performed by a fellowship-trained endocrine surgeon or an otolaryngologist specializing in head and neck cancer (N=11). Patients were blinded to their allocation until their pathology report was reviewed at their 2-week post-operative visit.

Assessment of Complications

Hypoparathyroidism—After surgery, all patients had a serum calcium and PTH levels checked in the recovery room, and then again at 2 weeks and 6 months post-operatively. Transient hypoparathyroidism, which was the primary endpoint of the study, was defined as a post-operative PTH level <10 pg/mL. All patients were treated empirically with calcium/calcitriol based on our institution’s calcium protocol [16], which recommends as needed calcium for symptoms of hypocalcemia for all patients, and scheduled calcium carbonate 1000 mg BID if their PTH <20 pg/mL. Calcitriol 0.25 mcg BID was added for a PTH <10

pg/mL and increased to 0.5 mcg BID for a PTH <4 pg/mL. At the 2-week post-operative visit, if both the calcium and PTH had normalized, medications were titrated off and labs repeated as indicated until the scheduled recheck at 6 months. Hypoparathyroidism was considered permanent if the patient required ongoing calcium or calcitriol treatment to prevent/treat symptoms > 6 months after surgery.

Voice and Swallow Assessment

All patients received pre-operative and postoperative (2 weeks) video laryngoscopies and stroboscopies in order to assess the function of the recurrent laryngeal nerve. All exams were re-reviewed by a blinded laryngologist. Vocal fold paralysis was defined as immobility of a vocal fold on direct laryngeal exam. Any vocal fold mobility changes from baseline exam (including subtle changes suggestive of possible superior laryngeal nerve injury) were considered “other vocal fold changes”. Laryngeal exams were repeated at 6 weeks, 6 months, and 1 year until they normalized or returned to baseline. Video swallow studies were performed preoperatively and at 2 weeks post-operatively in the first 37 patients, but were discontinued due to a lack of clinically relevant findings. Patients also completed validated QOL instruments specific to voice (Voice Handicap Index)[17] and swallow (EAT-10)[18] pre-operatively at 2 weeks, 6 weeks, 6 months and 1 year post-operatively.

Quality of Life and Patient Experience

Patients completed 3 Global QOL surveys at each of the 5 study time-points: the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 version 3[19], 12-Item Short Form Survey (SF-12) SF-12 [20] and the Thy-CA QOL [21] instruments.

Post-operative Treatment and Follow up

Given local practice patterns when the study started, our protocol administered radioiodine ablation (RAI) (50 mCi) to all patients with recombinant TSH stimulation 2–3 months after surgery. In 2016, the ATA Guidelines [3] stated that RAI was no longer indicated for low risk patients. Given this, the protocol was modified to no longer require RAI if the patient met the ATA definition of an “excellent response to therapy” at 6 weeks after surgery (definition below).

Tg levels were obtained at 6 weeks (prior to RAI), 6 months and 1 year after surgery and sTg levels were obtained at 6 weeks (prior to RAI) and 1 year. Cervical neck US was obtained at 6 months and 1 year and reviewed by an expert radiologist. Findings were classified as negative (no evidence of disease), structural evidence of disease (structural findings highly suggestive of disease), or non-specific findings (includes: changes related to surgery, nodes that are not 100% normal in appearance, findings that are too small to clarify, follow up was recommended).

Since the protocol had to be modified during the trial to allow patients with an “excellent response to therapy” to avoid RAI, we expanded our 1 year recurrence endpoints to use this ATA categorization to assess 1 year outcomes as it incorporated all of our available data to assess recurrence (Tg and sTg levels and US findings). All patients were classified into 4 categories based on the 2016 ATA Definitions for *Response to Initial Therapy* [3].

Excellent response to therapy: Negative Tg Antibody (TgAb), a Tg <0.2 ng/mL or a sTg of <1 ng/mL, negative imaging

Biochemical Incomplete Response: Negative imaging AND Tg $\geq$ 1 ng/mL or sTg $\geq$ 10 ng/mL or rising anti-Tg Ab levels

Structural Incomplete Response: Structural evidence of disease with any Tg level with or without Tg Ab

Indeterminate Response: Nonspecific findings on imaging studies, Tg detectable but < 1 ng/mL, sTg < 10 ng/mL or stable or declining anti-Tg Ab levels in the absence of structural disease on imaging.

Statistics

This RCT was designed with a power of 0.8 and an alpha of 0.05 to detect a 3 fold increase in the rate of a post-operative PTH < 10 pg/mL between the TT (assumed to be 12% based on historical data from our prospectively maintained institutional database) and the TT+pCND (estimated from the literature to be 36% [8, 22, 23]). Our initial recruitment goal was 116 pts. After 60 patients were randomized, an interim analysis revealed a higher rate of PTH < 10 pg/mL in our TT group, and calculations demonstrated that nearly 100% of the remaining patients in the CND group would have to develop a complication and no patients in the TT group, for us to demonstrate that CND had a statistically significant higher complication rate. Given this finding, it was felt that ongoing recruitment was unlikely to change our conclusion. Since analysis of our secondary endpoints demonstrated similar outcomes across all measures, it was deemed to be appropriate to end enrollment and proceed with data analysis. This study was never powered to show a difference in clinical recurrence rates, as previous work has shown that a much larger study with significantly longer follow up than is feasible within this funding mechanism would be required to show any differences between groups [14].

All statistical analyses were performed with SPSS (Version 26.0). Comparisons between groups were performed with a 2-sided Fisher's Exact test or independent samples t-tests. All reported data list the TT group followed by the TT+pCND group. QOL scores were compared between groups at each time point with independent t-tests followed by a mixed effect model comparing the relationship between treatment groups over time. Statistical significance was defined as alpha less than or = 0.05.

RESULTS

Patient Demographics

Sixty patients randomized to TT and TT +pCND were demographically similar at baseline and had similar pathologic features (TABLE 1). Tumors averaged 2.2 ± 0.2 cm and 11.9% had extra-thyroidal extension. Positive nodes were identified in 27.6% of patients undergoing a pCND (all ≥ 6 mm). Despite the TT patients not undergoing a formal lymph node dissection, 10% were found to have a positive node removed with the specimen.

Complications

There were no differences in the rates of vocal cord issues (recurrent laryngeal nerve paralysis or any mobility change from baseline) or in rates of transient hypoparathyroidism ($\text{PTH} < 10 \text{ pg/mL}$) based upon the performance of a pCND (FIGURE 2). Interestingly, both categories of complications trended higher in the TT alone group.

Post-operative calcium and PTH levels were equivalent between groups at all points (TABLE 1). PTH levels $< 10 \text{ pg/mL}$ were present in 28.8% of patients and the frequencies were equivalent between groups (FIGURE 2). By 6 months 82.4% of patients with a $\text{PTH} < 10 \text{ pg/mL}$ had resolved and 3 patients were considered to have permanent hypoparathyroidism.

Recurrent laryngeal nerve paralysis was present in 11.8% ($N=7$) of patients at 2 weeks which decreased to 3.4% ($N=2$) by 6 weeks. These 2 patients had not fully recovered by 6 months and were considered permanent. Voice Handicap Index surveys were administered at each time point and revealed similar trends with a slight increase at 2 weeks after surgery ($+8.46 \pm 3.22$ vs. $+8.33 \pm 4.53$, $p=0.98$) with a subsequent return to baseline by 1 year for both groups. EAT-10 Surveys were administered and showed a higher EAT-10 score in the TT group at 2 weeks (4.57 ± 1.08 vs. 1.93 ± 0.57 , $p=0.04$) but this difference resolved by 6 weeks and the results were equivalent at 1 year (0.76 ± 0.31 vs. 1.22 ± 0.54 , $p=0.46$). These scores were well below the threshold score of 3 (clinically significant swallowing issues), but remained above the normative value of 0.4 at 1 year in both groups.

Oncologic Treatment and Outcomes

Six weeks after surgery, prior to RAI, patients had both a Tg and sTg drawn (TABLE 2). Both groups were equally likely to achieve a $\text{Tg} < 0.2$ (54.5% vs. 66.7%, $p=0.54$) (FIGURE 3). An *excellent response to therapy* at 6 weeks was achieved equally amongst the groups (59.3% vs. 64.0%, $p=0.78$). Initially 100% of patient received an ablative dose (50 mCi) of RAI, but in the second half of the study, patients were allowed to forego RAI if they achieved an excellent response to therapy based on Tg levels at 6 weeks. RAI was administered to 66% of patients ($N=39$) and was similar between groups (73.3% vs 63%, $p=0.57$). RAI scan showed no evidence of distant disease in any patients. Mean % RAI uptake in the neck was $0.14 \pm 0.04\%$ and there was no difference between the groups ($p=0.50$).

At 6 months, a $\text{Tg} < 0.2$ was achieved at similar rates between groups (82.1% vs. 91.3%, $p=0.44$). Neck US were read as no evidence of disease in 66% of patients. At 1 year, rates of $\text{Tg} < 0.2$ (88.9% vs. 90.0%, $p=1.00$) and stimulated $\text{Tg} < 1$ (93.8% vs. 92.3%, $p=1.00$) remained equivalent. Only 1 patient in the pCND group had a $\text{sTg} > 2$. Neck US at 1 year were read as normal in 85.1 % of patients (85.7% in TT vs. 85.1% in CND, $p=1.00$). Questionable/unclear findings on US were present in both groups (10.7% vs. 14.8%, $p=0.70$), but only 1 patient in the TT group was found to have structural evidence of disease and a biopsy-proven recurrence in the lateral neck at 6 months (in retrospect that disease was present on the pre-operative US but was missed).

After combining the Tg and US data, patients were classified according to the ATA categories defining their response to therapy (FIGURE 4). An *excellent response to therapy* was achieved in 80.0% of patients undergoing a TT versus 80.8% undergoing a TT+pCND ($p=0.76$). No patients had a biochemical incomplete response and patients were equally likely to have an indeterminate response (16.6% vs 19.2%, $p=0.45$).

Quality of Life

The Global QOL EORTC showed a small improvement over time from baseline to 1 year for all patients ($p=0.0001$) but demonstrated no difference in QOL between the groups ($p=0.63$) (FIGURE 5A). The Thyroid Cancer specific QOL measure (ThyCA-QOL) revealed some inconsistencies between groups over time ($p=0.03$), but no overall difference between groups ($p=0.96$). (FIGURE 5B). The SF-12 also demonstrated no difference between groups over time in either Mental ($p=0.86$) or Physical Scores ($p=0.25$) (data not shown).

DISCUSSION

Microscopic lymph node disease that is clinically not detectable by preoperative imaging and intraoperative inspection is common in patients with PTC (27.6% in the current study). While removing these nodes prophylactically did not increase the risks of surgical complications, there was no clear clinical advantage to resecting this microscopic nodal disease. When comparing early markers of disease recurrence, patients did equally well after TT regardless of whether or not a pCND was performed.

In designing this study, we chose transient hypoparathyroidism, the most common complication after thyroidectomy, as our primary outcome. We chose the numeric definition of a PTH <10 pg/mL, because it was a discrete variable and could be measured shortly after surgery [24, 25]. Post-operative PTH levels are a reliable predictor of both symptomatic hypocalcemia and permanent hypoparathyroidism [25–28]. In this study, while this complication occurred in about a quarter of patients, most resolved within a few weeks, and when managed appropriately appeared to have minimal impact on QOL [29]. Based on previously published data we hypothesized that the rate of this complication would be significantly higher when a CND is performed, given the risk of de-vascularization of the lower parathyroid glands [8, 30–32]. Surprisingly, after enrolling 60 patients, this complication was actually more common in the patients undergoing a TT. Based on an interim analysis we surmised that ongoing enrollment of patients would not demonstrate a significantly increased risk of transient hypoparathyroidism with performance of a pCND. Given the changing landscape in the treatment of thyroid cancer since this trial was initiated, we felt it was best to report the results at this stage and to use the data we generated from this trial to help inform future research about the extent of surgery (lobectomy versus total thyroidectomy), the role of RAI, and the impact of complications on patient QOL [1, 12, 33].

Complication rates after thyroid surgery are often underreported; as the detection and frequency is dependent upon surgeon self-report and the methods used to screen/diagnose complications. In this study with all patients undergoing comprehensive voice evaluations the rates of voice changes were higher than previously reported [32, 34, 35] and surprisingly occurred more frequently in the TT group than in the CND group. Thankfully most of

these complications were transient (recovered by 6 weeks) and had a manageable impact on patient's QOL [36]. In reviewing data from the voice evaluations, it became clear that more subtle changes in vocal cord structure and function, that are not a true paralysis, can occur after surgery. The etiology, frequency, severity, and impact of those changes was highly variable among patients. Understanding the impact of thyroid surgery on patient vocal function and voice outcomes is an important part of the ongoing analysis of this study data [36].

While some studies have shown that performing a CND increases the risks of complications [6, 31, 37–39], other studies from high volume centers, have noted that when done by a high-volume surgeon the risks of a CND do not increase the risks of thyroid surgery [30, 40]. Although we did not find that a pCND increased the risks of surgical complications, we did show that even when done by an experienced and well-trained surgeon, the risks of these complications are higher than often reported [34]. Since the majority of thyroid surgery in the country is done by surgeons who perform a low volume of thyroidectomy (<25 cases)[41], the data from this study may not be extrapolated to all surgeons and it is possible that performing a pCND would increase complications if done by a surgeon with less experience.

To classify patients as having a prophylactic, and not a therapeutic CND, it is important that preoperative imaging accurately detect clinically significant nodal disease. Given the variability in US quality, for this study we required all exams to be reviewed by an expert radiologist prior to enrollment[42]. Since nodal disease, particularly in the central neck, can be missed preoperatively and identified intraoperatively, we also thought it was essential that patients not be randomized until after the surgeon had assessed the nodes intraoperatively. Despite doing this, microscopic nodal disease was still found in about 26% of patients undergoing a pCND. While we confirmed that removing these nodes would indeed identify microscopic disease, we could not demonstrate that removing these nodes impacted early markers of disease recurrence.

In previous retrospective studies, the challenge with examining outcomes after a pCND is that once the presence of nodal disease (even if microscopic) is documented, this upstages the patient and providers treat those patients with more RAI [33, 40]. In order to try to control for this variability, when our study was designed we required an ablative dose of 50 mCi of RAI for all patients. While this worked initially, in 2016, the new ATA guidelines [3] were published recommending avoidance of RAI in low risk patients. We felt it was important to try to control how and when RAI was utilized so that we could accurately analyze the impact of surgical management (pCND) on outcomes, and thus amended our protocol. While not every patient received RAI in this study, the utilization was equivalent across both groups.

The goal for treatment of any thyroid cancer should be to optimize the number of patients who achieve an “excellent response to initial therapy”. If patients can achieve this short term outcome, data supports that their long-term risk of recurrence is <2% [43, 44]. In our study we compared every short term measure of recurrence available within the first year of treatment and found that there were no differences between our treatment groups based

upon the extent of initial surgery. Since 66% of patients did receive RAI in this study, it is possible that CND alone would have conferred more benefits if that treatment had not been received, however, we did check Tg and sTg prior to RAI treatment and those results were also equivalent between groups.

While biochemical markers were equivalent at all time points between groups, approximately 20% of patients had indeterminate US findings at 1 year. Most of these findings were very small and it is unclear if these changes represented post-operative changes, disease that was potentially treated with RAI, or if this is microscopic disease that is going to translate into clinical significant disease recurrences in long-term follow-up. Ongoing follow up of this cohort is going to be important to address this important question. There was only diagnosed recurrence in this study, in the TT group, and that recurrence was in the lateral neck. After reviewing the US images from that patient, in retrospect, the node was present on the pre-operative imaging, but was missed by the radiologist. This highlights the importance of high quality pre-operative US in order to determine the most appropriate initial surgery but also the accuracy of pre-operative US to select patients with clinically significant nodal disease in the central neck.

As part of this study we also administered multiple QOL surveys. Two global QOL surveys (SF-12, Global EORTC) and one thyroid specific (ThyCA QOL) as well as a voice (VHI) and swallow specific survey (EAT-10) were performed. In none of these validated measures could we show any differences between the groups based upon extent of surgery. Based on this data, if complication rates are similar, the extent of surgery does not impact QOL.

Given the large amount of data collected as part of this prospective randomized controlled clinical trial, it was only performed at a single site. While having a single site improves the validity and consistency of the data collection, it does limit the generalizability of the findings. While the primary endpoint was to examine short term risks (low PTH after surgery), we also collected a large amount of data for secondary endpoints about the patient experience, quality of life and disease recurrence. This study was not powered to show a difference in long term clinical recurrence rates, but we collected data on surrogate markers of recurrence that can be used to predict long-term outcomes. We presented all of the surrogate markers collected to predict clinical recurrence and the data shows enough similarities at 1 year, that we think it is unlikely that with long term follow up we will see clinically meaningful differences between the groups.

CONCLUSION

Clinically node negative PTC patients treated with TT with or without a pCND had similar complication rates after surgery. Although positive microscopic nodes were discovered in 27.6% of pCND patients, oncologic outcomes were comparable at 1 year. While our data suggests that a pCND can be completed safely by a high volume surgeon, the benefit of performing a CND was not evident at 1 year. At 1 year, approximately 20% of patients in both groups had indeterminate lab or imaging findings and it is possible that this could translate into differences in long-term recurrence rates and this warrants ongoing study.

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FIGURE 1.
CONSORT Diagram

FIGURE 2.

Complication rates between treatment groups. * No significant differences between groups

FIGURE 3.

Short term cancer outcomes between treatment groups. There were no significant differences between groups on any of the measured outcomes.

FIGURE 4.

Groups categorized by the American Thyroid Association (ATA) Response to Initial Therapy

FIGURE 5A and 5B.

(5A) Global QOL EORTC for treatment groups over time compared to the global health status mean for the general population. (5B) QOL as measured by the THYCa-QOL for

treatment groups overtime. Data was collected at specified time points on the x-axis, lines are to demonstrate trends over-time for each cohort.

TABLE 1:

Demographics and Laboratory Findings

Variables	Total Thyroid (N=30)	Total Thyroid + Central Neck Dissection (CND) (N=30)*	p-value
Age (years)	46.1±2.5	50.1±2.4	0.26
Gender (%Female)	77%	75%	0.71
Baseline Calcium	9.5±0.1	9.5±0.09	0.97
Baseline PTH	60.5±6.0	52.5±6.4	0.37
Post-op Calcium	8.7±0.1	8.8±0.1	0.51
Post-op PTH	28.7±5.1	26.9±3.8	0.78
2 week Post-op Calcium	9.1±0.1	9.4±0.1	0.11
2 week Post-op PTH	38.6±5.3	35.3±6.7	0.71
6 month Calcium	9.0±0.1	9.1±0.1	0.54
6 month PTH	45.0±4.7	46.5±5.0	0.84
6 week Tg	0.5±0.2	0.3±0.1	0.36
6 week sTg	7.2±4.6	3.2±0.9	0.43
6 week Tg Ab present (%)	11.5%	8.0%	1.00
6 month Tg	0.5±0.4	0.1±0.0	0.33
6 month Tg Ab present (%)	6.7%	8.0%	1.00
1 year Tg	0.2±0.1	0.1±0.1	0.57
1 year sTg	0.3±0.1	0.5±0.4	0.47
1 year Tg Ab present (%)	0.0%	4.2%	0.46

* 1 additional patient was initially randomized top CND but found to not have cancer on final pathology and was excluded from all analyses

TABLE 2

Pathology

Variable	Total Thyroid (N=30)	Total Thyroid + Central Neck Dissection (CND) (N=30)*	p-value
Tumor Size (cm)	2.45± 0.26	1.91±0.21	0.12
Multifocal	13 (43.3%)	14 (48.3%)	0.80
Extra-thyroidal Extension [#] (ETE)	4 (13.3%)	3 (10.3%)	1.00
Vascular Invasion	1 (3.3%)	5 (17.2%)	0.10
High Risk Pathology	1 (3.3%)	1 (3.4%)	1.00
Follicular Variant of PTC	6 (20.0%)	4 (13.7%)	0.73
Positive Margins	2 (6.7%)	2 (6.9%)	1.00
Tumor Staging			
T1 Tumor	13 (43.3%)	18 (62.1%)	0.20
T2 Tumor	10 (33.3%)	7 (24.1%)	0.57
T3 Tumor (>4 cm or ETE)	7 (23.3%)	4 (13.7%)	0.51
# of lymph nodes (LN) removed	0.77±0.24	7.10±0.92	<0.001
Positive Nodes	10.0%	27.6%	0.10
Largest Positive node (cm)	0.30±0.1	0.41±0.05	0.33
# of Positive LN	0.40± 0.24	1.66±0.67	0.09

[#] ETE was invasion into the strap muscles, there was no gross ETE into surrounding organs identified

* 1 additional patient was initially randomized to CND but found to not have cancer on final pathology and was excluded from all analyses