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Unifocal Differentiated Thyroid Cancer Smaller than 1 cm are Better Managed by Total Thyroidectomy

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Abstract

Background: The optimal extent of surgery for differentiated thyroid cancers (DTC) is controversial. The aim of this study is to assess the frequency and potential predictive factors of residual malignancy in the lobe contralateral to the main tumor. The secondary aim was to assess the safety of completion thyroidectomy.

Methods: All total thyroidectomies performed at our institution between 2004-2010 were reviewed identifying 185 patients (70 cases underwent completion thyroidectomy and 115 cases underwent initial total thyroidectomy). The predictive value of sex, age, tumor size, histology, multifocality, perithyroid extension, and lymph node involvement was analyzed.

Results: we report a high rate of multifocality (51%) in the whole cohort of cases and of contralateral disease (35%). There were no differences in multifocality rates for sex, age, pathology types and tumor size. PTC cases < 1cm have a similar contralateral disease to cases > 1 cm (45% versus 59% respectively). Moreover, there was no significant correlation between ipsilateral multifocality and contralateral disease in our cases. In our series, the complication rates for both completion thyroidectomy and total thyroidectomy were comparable.

Conclusion: Absence of significant predictive factors that could suggest a residual disease justifies total thyroidectomy as a primary treatment for cases of DTC. Hemithyroidectomy for management of cases of DTC smaller than 1 cm with absence of multifocal disease in the ipsilateral lobe should be questioned.

Keywords: Differentiated thyroid cancer; Total thyroidectomy; Completion thyroidectomy; Multifocal carcinomas

Introduction

Although controversy exists regarding the extent of surgery in patients with differentiated thyroid cancer of follicular origin which includes papillary, follicular, and Hurthle cell malignancies, there is general agreement that a total thyroidectomy is indicated in patients considered to be high risk [1,2]. Approximately 90% of all thyroid cancers are well differentiated and of follicular origin and approximately 80% of these tumors are staged as low risk [3].

Thyroid lobectomy has been considered as adequate therapy for a papillary thyroid carcinoma (PTC) in a low-risk patient that is less than 1.0 cm (papillary micro carcinoma, mPTC), is confined to the thyroid gland, does not have insular or tall cell features and does not demonstrate angioinvasion or metastasis. A completion thyroidectomy would, therefore, not be indicated in this group of patients. Patients with this PMC have a death rate of 0.1% and a recurrence rate of 5% [4]. For follicular thyroid carcinoma, the absence of multicentric disease is an argument against bilateral thyroidectomy for management of primary tumors. However, other authors recommend complete removal of all thyroid tissue in all case of differentiated thyroid cancers (DTC) at least to facilitate subsequent radioactive iodine therapy [5].

Among the main considerations for the limited surgery recommendations is the estimated low rate of tumor multifocality in the thyroid gland and more specifically in the contralateral lobe. Several studies established a clear association between tumor multifocality and local recurrence, regional recurrence, and lymph node involvement, and distant metastases. Hence the need for a more aggressive approaches [6-8]. The incidence of multifocality is understudied and ranges between 18% and 87% with some of the studies dated more than 4 decades ago [7-11].

Although the debate is still going, once the diagnosis of DTC is made in one lobe many physicians think that a completion thyroidectomy should be considered to achieve total surgical ablation of thyroid [12, 13]. Completion thyroidectomy not only deals with residual carcinoma in the opposite lobe, but also facilitates I^{131} whole-body scanning, allowing for the diagnosis and treatment of unrecognized metastatic carcinoma [13]. However, the morbidity after completion thyroidectomy is reported to be many times more than the primary procedure [14], only a few studies reporting comparable morbidity for these two procedures [15]. As a protocol at our centre, we recommend patients for completion thyroidectomy if they are referred to us after subtotal thyroidectomy or the diagnosis of thyroid cancer is confirmed after hemithyroidectomy.

The primary objective of this study is to assess the frequency of malignancy in the residual thyroid tissue removed after completion thyroidectomy. Furthermore we analyzed a number of clinical parameters as potentially predictive factors that may anticipate the presence of malignancy in the residual thyroid tissue. The secondary objective was to review our institution's experience with completion thyroidectomy in the management of DTC and to compare the results of recurrent laryngeal nerve (RLN) injury, and hypocalcaemia against a cohort of patients treated by primary total thyroidectomy.

Patients and Methods

Patients

We reviewed the medical records of 343 patients who underwent

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total thyroidectomy in our institution in the period between 2004 and 2010. After exclusion of 132 cases that underwent treatment for benign diseases and 26 cases that lost follow up, our cohort included 185 patients with DTC. Seventy cases underwent completion thyroidectomy. Among those cases, 56 patients were referred to our center from other hospitals. Fourteen cases underwent initial surgery at our clinic for benign goiter or adenoma which was diagnosed as DTC at postoperative biopsy. Preoperative investigations included estimation of serum thyroxin (T4) and thyroid stimulating hormone (TSH), calcium, neck US, radioactive thyroid scan and indirect laryngoscopy. The TNM classification system was used for staging. FNAC was performed to all cases in our institute preoperatively. For cases referred to our center from other hospitals, the following data were collected: size of the initial tumor, location, radiologic status of the residual thyroid tissue and cervical LNs and postoperative pathology. Slides of the initial surgery were revised with special emphasis on multifocality.

Surgical technique

For total thyroidectomy, the capsular dissection method was used. The external branch of the superior laryngeal nerve was saved by individual ligation of vessels in the upper pole. An attempt was made to follow the course and preserve both recurrent laryngeal nerves and four parathyroids. However, we took care not to dissect the parathyroids out of their fatty envelopes. The blood supply to the parathyroids was preserved by ligating the individual branches of the inferior thyroid artery on the capsule of the thyroid. When there was inadvertent injury to the parathyroid glands or their blood supply, they were auto transplanted in the sternocleidomastoid muscle on the same side.

Completion thyroidectomy was done within 7 days of the initial operation or after 6 weeks. When re-opening the operative site, particularly if this is performed in the early postoperative period, the thyroid bed should be thoroughly rinsed with saline before dissection for removal of clots or debris. All cases were performed via the lateral approach. The carotid sheath is retraced laterally, the omohyoid muscle is transected, and the lateral thyroid is approached. Harmonic Scalpel has been used routinely in our center since 2006 and is effective in reducing operative bleeding, operating time and facilitating meticulous dissection. When re-operating on the ipsilateral thyroid gland, the recurrent laryngeal nerve is often difficult to identify and dissect as it is buried in scar tissue. Palpation of the cricothyroid junction and the inferior cornu of the thyroid cartilage was helpful to identify the nerve just anterior to this point and it can then be traced inferiorly. Any structure that is suggestive of being a parathyroid gland should be considered as such until proven otherwise.

Central lymphadenectomy (removing level VI pretracheal and paratracheal LNs) was routinely performed. Dealing with lateral cervical LNs (level II-V) depended upon the preoperative clinical and radiologic assessment. When preoperative examination indicated positive LNs, functional neck dissection (removing nodal levels, II, III, IV, and V with preservation of the internal jugular vein, sternocleidomastoid muscle and spinal accessory nerve) was performed. For those who showed negative results in preoperative imaging, lateral neck nodes were explored at surgery and any palpable LN was sent for frozen section examination. Cases that showed positive frozen underwent lateral neck dissection.

Postoperative I^{131} whole body scans were done to all patients after 4-6 weeks to detect residual thyroid tissue and to exclude functional metastases. Ablative doses (80-100 mCi) of I^{131} were given, if the uptake in the thyroid bed was greater than 1.5%. Subsequently, all patients were given hormone suppressive therapy (Eltroxin 200-300 mcg per day) and were closely monitored by FT3, FT4 and TSH aiming to keep TSH level below 0.1μIU/ml. Follow-up was done every 6 months by I^{131} whole body scan, neck ultrasound, and non-contrast CT chest.

Pathologic evaluation

The histopathology reports (including reports of the initial surgery that were revised in our center) were analyzed for the following information

Tumor subtype was noted as papillary carcinoma, papillary carcinoma–follicular variant, follicular carcinoma, or Hurthle cell carcinoma.

Tumor size with the largest tumor considered the primary tumor.

Focality: Patients were divided into 2 groups: single lesion and multiple lesions. The second group was then further subdivided to 3 subgroups: lesions located only at the same lobe as the main tumor (ipsilateral), lesions located at the other lobe (contralateral), and lesions located in both lobes (bilateral). The number and size of all tumors were also registered.

Perithyroid tumor extension: Defined as positive or negative.

Node status: Graded as positive or negative and number of nodes involved.

The following factors were analyzed as potentially predictive factors for presence of malignancy in the residual thyroid tissue and/or cervical LNs: age older than 40 years, gender, tumor pathologic type, size of the primary tumor, evidence of perithyroid tumor extension, lymph node status, and ipsilateral multifocality.

Procedure related complications

The complications with completion thyroidectomy were compared with the primary total thyroidectomy. We gathered data regarding wound infection, hematoma, seroma, RLN injury (temporary or permanent), and hypoparathyroidism (temporary or permanent). Temporary RLN injury was defined as a new onset vocal cord paralysis, identified in the postoperative period that was noted to recover completely at subsequent visits. Injuries were deemed permanent if paralysis persisted past 12 months from operation. Permanent hypoparathyroidism was diagnosed as either an unrecordable or abnormally low serum parathormone level, with a persistent dependence on vitamin D and calcium replacement at 6 months postoperatively. Temporary hypoparathyroidism was defined as hypocalcaemia in the immediate postoperative period requiring treatment with calcium, vitamin D, or both, which was eventually withdrawn.

NB Statistical analysis

Statistical analysis was done using the two tailed Fisher's exact test with the use of statistical software SPSS version 11.5 (SPSS, Inc, Chicago, IL) and a P value < 0.05 was considered to represent statistical significance for all comparisons.

Results

The final cohort of patients in the current study included 185 patients with WDTC, 70 cases underwent completion thyroidectomy, and 115 cases underwent initial total thyroidectomy. In the completion group there were 52 women and 18 men, with a mean age of 42.8 years. In the initial total thyroidectomy group there were 86 women and 29 men with a mean age of 46.2 years (Table 1). The difference between both groups regarding the age and gender was statistically insignificant (P=0.4 and P = 0.67 respectively).

Completion thyroidectomy group

Most cases (n =52, 70%) in the completion group were referred from other hospitals. Preoperative FNAC was performed to 26 cases (all 18 cases that were operated initially in our center and 8 cases referred from other hospitals). FNAC demonstrated follicular lesion in 5 cases, papillary carcinoma in 1 case, colloid goiter in 16 patients, suspicious smear in 2, and non representative in 2 cases. The primary operation in these cases were hemithyroidectomy (n=45), subtotal thyroidectomy (n=18), or subtotal lobectomy (n=7). The neck nodes were assessed in only 11 cases; 8 cases underwent unilateral modified radical neck dissection and 3 cases underwent lymph node sampling. Nodes were positive in all 8 cases of neck dissection and in 1 case of LN sampling. Final pathology reports in these patients revealed papillary carcinoma in 43 cases, follicular variant of papillary carcinoma in 12 cases, follicular carcinoma in 11 cases and Hurthle cell carcinoma in 4 cases. The median tumor size was 2.3 cm (range 1.2-6.7 cm). Tumors were single in 53 cases (76%) and multifocal in 17 cases (24%). Multifocal tumors were present in 10/52 cases who underwent hemithyroidectomy or lobectomy (ipsilateral), and in 7/18 cases who underwent subtotal thyroidectomy (3 bilateral, 1 ipsilateral, and 3 contralateral).

Completion thyroidectomy was performed within a median of 3.1 month (range 12 days- 5 months). The previously resected lobe had to be explored in 22 patients because of the presence of radiologic evidence of residual thyroid tissue. Residual tumor was found in 27 specimens after completion thyroidectomy; 14 contralateral, 3 ipsilateral, and 10 bilateral. The median tumor size was 0.7 cm (range: 0.2-2.1 cm). Cervical lymph node status was negative clinically and radiologically in 57 cases and positive in 13 cases. Intraoperatively, nodal metastasis was suspected in 9 patients (of the 57 radiologically node negative cases), and confirmed by frozen section examination in 6 cases. Modified radical neck dissection was performed in 19 patients, bilateral in 5 and unilateral in 14 cases. Final node positive cases after both surgeries were 28. Overall, on pathologic examination of specimens obtained from both the initial surgery and completion surgery, a total of 40 multifocal cases was obtained (13 ipsilateral, 10 bilateral, and 17 contralateral). Multifocality was significantly correlated only with LN stratus. Multifocal tumors were present in 79% of node +ve cases (22/28) and in 43% of node –ve cases (P= 0.03)

The contralateral lobe showed residual tumor tissue in 27 patients (39%). None of the predictive factors analyzed for contralateral disease reached a statistical significance.

Complications of the second surgery were as follows: 15 patients had transient hypocalcaemia that needed oral calcium supplement for less than a month. 1 patients had permanent hypoparathyroidism that needed long term treatment with oral and IV calcium. Temporary RLN palsy was found in 2 cases, and only 1 case had permanent RLN

	Completion thyroidectomy Group (n=70)	Total thyroidectomy Group (n=115)	Total (n=185)
Age			
< 40 years	32	53	85
>40 years	38	62	100
Sex			
Males	18	29	47
Females	52	86	138
FNAC			
Follicular lesion	5	21	26
Papillary carc	1	49	50
Colloid nodulre	16	16	32
Suspicious	2	19	21
Non respresentative	2	10	12
Lymph Nodes			
Status			
+ve	28	52	80
-ve	42	63	105
Operation			
Mod Neck Dissection	27	51	78
Berry picking	3	5	8
Final Pathology			
Papillary Ca	43	72	115
Follicular variant Papillary ca	12	25	36
Follicular ca	11	15	26
Hurthjle cell ca	4	3	7
Mean tumor size	2.2 cm (0.2-6.7cm)	2.6 cm (0.7- 6.3 cm)	
Perithyroid tumor extension			
+ve	14	22	36
-ve	56	93	149
Multifocal tumors			
Ipsilateral	13	17	30
Contralateral	17	13	30
Bilateral	10	25	35
Comtralateral lobe			
Positive	27	38	65
Negative	43	77	120

Table 1: Clinicopathologic data of completion and total thyroidectomy groups.

injury. This case underwent ST as the primary operation outside our institution (Table 2).

Primary total thyroidectomy group

115 cases underwent initial total thyroidectomy. Preoperative FNAC was performed to all cases. It demonstrated follicular lesion in 21 cases, papillary carcinoma in 49, suspicious smear in 19 cases, colloid goiter in 16 and non representative in 10 cases. Final pathology was papillary carcinoma in 72 cases, follicular variant of papillary carcinoma in 25 cases, follicular cancer in 15 cases and Hurthle cell carcinoma in 3 cases. The mean tumor size was 2.6 (range: 0.7-6.3 cm). Single lesion was identified in 60 patients as opposed to 55 patients with multifocal disease. Patients with multifocal disease were further classified into ipsilateral lesions only (n= 17), contralateral only (n=13), or bilateral (n= 25). The neck nodes were assessed in 56 cases; 43 cases underwent unilateral modified radical neck dissection and 8 cases underwent bilateral MRND, and 5 cases underwent lymph node sampling. Cervical lymph node metastasis was present in 52 cases. Multifocality was present in 69% of node positive cases (n=36) and in 30% of node negative cases (n=19) with a significant P value (P=0.01).

The overall morbidity after the 115 primary total thyroidectomy included temporary hypocalcaemia in 24 cases (21%), permanent hypocalcaemia in 2 cases (2%), temporary hypoparathyroidism in 3 cases (3%), seroma in 5 cases and 1 case developed wound infection that was managed by antibiotics. Comparison of complications of both groups is illustrated in table (2).

Final histopathologhic report of the entire cohort of patients (n=185) revealed 115 cases with papillary carcinoma, 37 with follicular variant of papillary carcinoma, 26 with follicular carcinoma, and 7 with Hurthle cell carcinoma. The overall rate of multifocality is 51% (n=95). Multifocal cases were ipsilateral (16%, n=30), contralateral (16%, n=30), or bilateral (19%, n=35). Multifocality was only significantly affected by LN positivity (P= 0.02). The rate of contralateral positivity was not significantly correlated with any of the predictive factors assessed including tumor multifocality. Contralateral lobe was positive for malignancy in 65 cases (37%); 30 cases were +ve despite the absence of focality in the ipsilateral lobe, and 35 +ve in presence of multifocality in the ipsilateral lobe (P=0.3) (Table 3).

Follicular carcinoma cases occurred more in males (19/26) and in older age groups (20 cases were > 40 years). The tumor size in follicular carcinoma cases tend to be larger [mean 2.3 cm (range: 1.4-5.6 cm) versus a mean of 1.9 cm in papillary cancer cases (range: 0.2-6.7 cm)]. Furthermore, multifocality was present in 9 cases (35%) of follicular carcinoma (7 +ve contralateral lobe) that was once considered a unifocal disease. Most of these tumors were found to be PMCs with 68% measuring <1cm. Hurthle cell carcinoma was present in 7 cases, 2 cases showed ipsilateral multifocality.

Papillary carcinoma group (including follicular variant of papillary carcinoma) included 152 cases. The rate of multifocality in PTC cases was 51% (77/152). Patients were analyzed in 2 groups; those with tumors ≥ 1cm (n=105, 69%) and those with tumors < 1 cm (n= 47, 31%). No significant difference existed between both groups in age or sex. Multifocality was present in 62 cases (59%) with tumors ≥ 1cm (44 cases showed +ve contralateral lobe) and in 21 cases (45%) with tumors < 1 cm (13 cases showed +ve contralateral lobe) (P=0.3) (Table 4).

Complication	Completion thyroidectomy (n=70)	Initial Total thyroidectomy (n=115)
Temporary hypoparathyroidism	15 (21%)	24 (21%)
Permanent hypoparathropidism	1 (1%)	2 (2%)
Temporary RLN palsy	2 (3%)	3 (3%)
Permanent RLN palsy	1 (1%)	0
Hemorrhage	1 (1%)	0
Wound infection	2 (3%)	1 (1%)
Seroma	4 (6%)	5 (4%)

Table 2: Complications of completion thyroidectomy and initial thyroidectomy groups.

Discussion

The preoperative diagnosis o f DTC can be defined with FNA if the tumor is greater than 1 cm in size, total thyroidectomy in the treatment of choice for the treatment [16]. The controversy exists for the treatment of tumors less than 1 cm in diameter and where the diagnosis is made after hemi- or partial thyroidectomy for thyroid nodule. Options include completion thyroidectomy or I^{131} ablation. However the later approach is associated with many disadvantages, including multiple doses of I^{131} for successful ablation, difficulty in ablating large thyroid residue. In addition, high doses of radioactive iodine can result in pulmonary fibrosis, temporary bone marrow suppression and leukemia [17]. Therefore surgical resection remains the best way to remove the remnant thyroid tissue. Ideally, if one could identify with high accuracy the extent of the disease and be able to excise all malignant tissue leaving only normal thyroid tissue, the issue might be resolved. However, this goal is not attainable with the current diagnostic techniques. In view of that limitation, interesting questions that may arise would be "How frequent is residual malignancy in patients who had partial thyroid surgery?" and "Could one predict its presence in any given patient?" [18].

The incidence of separate malignant lesion at completion thyroidectomy following the initial thyroid lobectomy ranged in the literature from 31 to 77% and lymph node metastases ranged from 17 to 40% [18-20]. Although studied for several decades the exact incidence and ramifications of multifocal disease, and more specifically contralateral disease, is not well established for 2 reasons. First, some patients undergo unilateral lobectomy only, so that no information is available on the contralateral lobe. Second, there is some inconsistency regarding the terminology. Multifocal disease, defined as more than 1 cancerous lesion, can be located in the ipsilateral lobe only and should not be mistaken for contralateral disease. Published data, some of which is 4 decades old, cite multifocality to occur between 18% and 87% [7- 11]. However, the rate of contralateral disease is estimated as 13% to 56% only [21,22]. In a more recent study, Pitt et al identified a rate of 29% for contralateral disease in a cohort of 228 patients [11]. In our single-institution study in a cohort of 185 patients with DTC, we report a total rate of 51% multifocality and 35% contralateral disease. Our data failed to find any influence on multifocality or on the rate of contralateral disease by age, sex, and pathology subtype or tumor size.

Papillary thyroid cancer is known to be multifocal in about 30–80% [20,23], thus initial total thyroidectomy remains an effective and safe treatment method to reduce the surgical risk of the patients and facilitate to perform radioactive iodine therapy. Follicular thyroid cancer tends to be less multifocal than papillary thyroid cancer does but they are much more aggressive and, if they are widely invasive or extra thyroidal disease is found, completion thyroidectomy should also be performed [24].

The reported rates of the incidence of contralateral PTC discovered in completion thyroidectomy or total thyroidectomy specimens ranges from 13% to 56% [21,25]. Regarding mPTC, 28% of patients have been reported to have PTC in the contra lateral lobe on histological review [21,26]. Our series is consistent with these previous reports. Thirty six percent (n= 57/152) of all patients and 42% (n= 44/105) of patients

	Contralateral lobe –ve (n= 120)		Contralateral lobe +ve (n=65)		P value (for contralateral disease)
	Ipsilateral multifocality -ve (n=90)	Ipsilateral multifocality +ve (n=30)	Ipsilateral multifocality -ve (n=30)	Ipsilateral multifocality +ve (n=35)	
Age					
< 40 years (85)	46 (54%)	13 (15%)	12 (14%)	14 (16%)	
> 40 years (100)	44 (44%)	17 (17%)	18 (18%)	21 (21%)	0.61
Gender					
Males (47)	26 (55%)	6 (13%)	8 (17%)	7 (15%)	
Females (138)	64 (46%)	24 (18%)	22 (16%)	28 (20%)	0.36
Perithyroid extension					
-ve (149)	74 (50%)	25 (17%)	23 (15%)	27 (18%)	
+ve (36)	16 (44%)	5 (14%)	7 (19%)	8 (23%)	0.29
LN status					
-ve LN (105)	66 (63%)	8 (8%)	14 (13%)	17 (16%)	
+ve LN (80)	24 (30%)	22 (28%)	16 (20%)	18 (22%)	0.09
Pathology					
Papillary carcinoma (152)	69 (45%)	25(16%)	27(18%)	31 (20%)	
Follicular carcinoma (26)	16 (62%)	3(12%)	3 (12%)	4 (15%)	0.12
Hurthle cell carcinoma (7)	5 (71%)	2 (29%)	0	0	

Table 3: Predictive factors of residual malignancy correlated with ipsilateral multifocality in the whole cohort of patients (n= 185).

	Single lesion	Multiple lesions			P for contralateral disease
		Ipsilateral	Contralateral	Bilateral	
<1cm (47)	26 (55%)	8 (17%)	6 (13%)	7 (15%)	0.33
>1cm (105)	43 (41%)	18 (17%)	20 (19%)	24 (23%)	

Table 4: Multifocality in papillary thyroid carcinoma cases (n= 152) according to tumor size.

with primary tumors >1 cm had contralateral PTC. Interestingly, patients with primary tumors < 1cm had a similar rate of contralateral disease (28%). These data suggest that the rate of contralateral PTC is independent of primary tumor size. In a review of 150 patients who underwent completion thyroidectomy, Grigsby et al also found that the size of the primary tumor did not predict the presence of contralateral disease [27].

Although 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 to better identify which patients would benefit from completion thyroidectomy when PTC is discovered incidentally after lobectomy. In completion thyroidectomy specimens, positive lymph node metastases at the initial surgery and a longer time interval between lobectomy and completion thyroidectomy have been associated with PTC in remaining lobe [28]. In addition, infiltration of the thyroid capsule, "tall-cell" variant, and the presence of a tumor capsule have been linked to bilateral PTC. Another variable shown to be predictive of PTC in the contralateral lobe is ipsilateral multifocal disease [24].

Tumor multifocality has been reported previously to correlate with the presence of the disease in the contralateral lobe [7] and with a higher risk of tumor recurrence [29]. In our study, we report a multifocality rate of 49%; ipsilateral only in 16%, contralateral only in 16% and bilateral in 17%. There was no significant correlation between ipsilateral multifocality and +ve contralateral lobe. Contralateral disease occurred in 30 cases in absence of ipsilateral multifocality versus 35 in presence of ipsilateral multifocality.

The absence of significant correlation between ipsilateral multifocality and contralateral disease could be explained by two reasons. First: multifocal disease has been considered for years an intraglandular spread of the primary tumor and hence regarded as more aggressive disease with increased risks of locoregional recurrence, as well as lymph node and distant metastases [6-8]. Recent advances in molecular genetics allowed investigators to challenge the assumption of intraglandular spread. In the last 5 years a few studies explored the genetic origin of mPTC. Shattuck et al [30] published their data in 2005 proving that tumor foci in patients with mPTC arose in 5 of 10 patients as independent tumors. Independent clonal origin was also observed by Park et al [31] in 2006 and Giannini et al [32] in 2007. This finding strengthens the argument of performing total thyroidectomy or completion thyroidectomy for tumors< 1 cm. Similarly, our findings in patients with follicular carcinoma also support this observation. Follicular carcinoma is considered a unifocal tumor that spreads to the bloodstream as opposed to the intraglandular route. Nevertheless, in 35% of our follicular carcinoma patients multifocal disease was identified. However, these were found to be mPTCs with 68% measuring <1cm. These are all obviously incidental independent clones, unassociated with the original, main follicular carcinoma.

Second: pathology guidelines for thyroid specimen examination recommend that only representative sections of the entire gland should be examined. At our institution, pathologists follow these recommendations. Mazeh et al [33], suggested that entire gland examination rather than representative seconds offers a superior representation and better diagnosis of multifocality (64% versus 54%, P=0.16) and more specifically bilateral disease (60% vs 37%, P= 0.04).

Despite the high frequency of malignancy on second surgical exploration, an important question would be the significance of this finding. Alzahrani et al [18] in his study stated that the median tumor size on second surgery was 0.8 cm, and only a minority of cases showed evidence of perithyroidal extension (7 cases) or soft tissue invasion (2 cases). Some investigators argue that such small residual tumors have little bearing on the patient's outcome [34]. Others have reported

higher recurrence rates and higher chances of pulmonary metastases [35] and other distant metastases. The policy in our institution calls for completion thyroidectomy in most cases of DTC with significant residual thyroid tissue. Because of this policy and because of absence of control group in which completion thyroidectomy was not done, we cannot draw a conclusion on the long term impact of completion thyroidectomy in patients with DTC.

One of the most feared complications of repeated thyroid surgery is RLN injury. Beahrs and Vander toll [36] found a 17% incidence of vocal cord paralysis in 548 secondary thyroidectomies. At the time of reoperation, the surgeon usually does not know if 1 or several parathyroid glands have been unintentionally removed with the thyroid. Furthermore, even if they are left in place, it is not possible to predict the functional value of the remaining parathyroid glands that may have been devascularized during the previous surgery. As technique and experience have improved, this incidence of complications has gradually decreased. We report a low complication rate with cases of completion thyroidectomy that was comparable to those of initial total thyroidectomy. Our data cope with Chao et al. [12] who reported a 2.6% incidence of transient RLN palsy in completion thyroidectomy. Mishra and Mishra. [37] reported that the incidence of transient RLN palsy was 4% and there was no permanent RLN palsy.

Conclusion

In this study, we report a high rate of 51% multifocality and 35% of contra lateral disease. We also show that the rate of contralateral thyroid cancer of patients with tumors > 1cm are similar compared with those having tumors < 1 cm. Moreover we failed to find a significant correlation between the factors commonly used for thyroid cancer staging including ipsilateral lobe multifocality and the occurrence of contralateral cancer. Therefore consideration for TT or CT should be made in cases of DTC regardless the tumor size or ipsilateral multifocality. Completion thyroidectomy is a safe procedure with low complication rates that are comparable to initial TT.

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