ORIGINAL ARTICLE

TOTAL/NEAR-TOTAL VERSUS HEMI-THYROIDECTOMY FOR LOW-RISK WELL DIFFERENTIATED THYROID CANCER: A RETROSPECTIVE STUDY

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Abstract

Background: There is a controversy regarding management of low-risk well differentiated thyroid carcinoma (WDTC) between total/near-total thyroidectomy (TT) and hemi-thyroidectomy (HT) due to the excellent prognosis and the indolent course of the disease. This study aimed to review the outcome of TT in comparison with HT in management of low-risk WDTC.

Patients and Methods: A retrospective evaluation identified 156 patients with low-risk WDTC between 2000 and 2011 comparing mainly the outcomes after either TT or HT.

Results: Mean age was 42.8± 4.12 years, of these 18% were males and 82% were females. Permanent recurrent laryngeal nerve palsy (RLNP) and permanent hypocalcemia were significantly higher in TT group (*P*=0.035) and (*p*=0.049) respectively. Mean follow-up was 8.5 years. Recurrence rate was significantly higher in HT group (*P*=0.002). Completion thyroidectomy related morbidity was more in HT group than the primary surgery (*P*=<0.001). At the time of the last follow-up, 94.2% of TT group, and 88.9% of HT group were alive.

Conclusion: TT, with postoperative ^{131}I and thyroid hormone supplementation was associated with more favorable outcome than HT alone.

Keywords: Conservative thyroidectomy, Thyroid surgery, Thyroid neoplasms.

INTRODUCTION

Thyroid carcinoma accounts for 1% of all human cancers[1] and represents 90% of all endocrine malignancies.[2] WDTC occurs in 90% of cases with the majority (approximately 70%) occurs in women.[3] Usually most patients with WDTC (>70%) are in the low-risk group.[4]

Surgery is the only effective treatment for the majority of cases.[5] There is controversy about the extent of surgery between conservative and TT according to the stage of disease and risk stratification defined by different systems of prognostic indicators e.g. AGES (age, histological grading, extrathyroid extension, size of the primary lesion) & AMES (age, distant metastasis, extra thyroid extension, size of the primary lesion) systems.[6]

The good results of TT, about 80% of patients with

WDTC are cured after initial therapy,[7] makes it the optimum surgical management. Complete removal of the thyroid allows ablation of the remaining normal thyroid tissue using ^{131}I and allows better therapeutic use of ^{131}I which in turn decreases recurrence and may also decrease cancer mortality.[8] Also complete removal of thyroid improves the value of postablation ^{131}I whole body scan (WBS) and allows follow-up of serum thyroglobulin (Tg) as a tumor marker.[9] But the high incidence of surgical complications in non-experienced hands and nonaggressive behavior of the disease have led others to recommend HT in low-risk WDTC, as complications would be lower even in hands of inexperienced surgeons and most patients are also euthyroid postoperatively, so no need for L-thyroxine replacement.[10] Still tumor recurrence occur at significantly higher rates after HT than after TT,[11] so there is a tendency for completion thyroidectomy at a later date with its more pronounced complications, and there is a risk of developing undifferentiated thyroid cancer within the thyroid remnant,[6] these add to the controversy.

Neck dissection is considered depending on the cervical lymph node status. ^{131}I is taken postoperative to ablate residual thyroid tissue after TT for WDTC and to ablate metastatic lesions anywhere.[12]

Aim of the work: Our study aimed to review the outcome of HT (as a conservative surgery) in management of low-risk WDTC and compare it that of TT.

PATIENTS AND METHODS

From January 2000 to December 2011, 156 patients were treated at Sohag University Hospital, stratified as low-risk WDTC according to Hay; women <50 years, men <40 years, WDTC, confined to the thyroid, and with a tumor diameter of 1-4 cm[13] i.e. not more T2 (<4cm) N0M0 according to TNM staging.[14] Patients were excluded if they were <20 years, had any previous irradiation to the head and neck, had metastatic cervical lymphadenopathy, papillary cancers with unfavorable histology or with psammoma bodies, and widely invasive or poorly differentiated follicular cancers.

Data taken from records included age, gender, histological variant, physical findings like association with benign thyroid diseases (hyperthyroidism, simple goiter), and symptomatology considering the condition whether a solitary thyroid nodule or multinodular goiter (dominant nodule). Surgical complications especially RLNP and hypocalcaemia, also survival rate, mortality and recurrence were also recorded.

Specific diagnostic evaluation was accomplished by means of ultrasonography (US), serum thyroid hormones, serum calcium, and laryngoscopy. Specific pathologic preoperative diagnosis was made by core biopsy and fine needle aspiration biopsy (FNAB).

Patients were divided into two groups according to the adopted surgery; group 1 included patients who underwent HT and group 2 included patients who were treated with TT.

In patients who underwent TT, the completeness of surgery was verified by ^{131}I thyroid scan 4 to 6 weeks after surgery before administration of postoperative L-thyroxine replacement therapy. At this time a WBS was performed, and when resident thyroid tissue was found an ablative dose of ^{131}I was given. A post-ablation WBS should be performed 3-10 days after the ^{131}I dose. A therapeutic dose was given to patients in whom locoregional recurrence or distant metastases developed.

Group 2 and group 1 patients who suffered permanent postoperative hypothyroidism received thyrotropin (TSH) suppressive doses of L-thyroxine. Replacement is titrated according to follow-up thyroid function tests obtained 6 to 8 weeks later.

Patients were followed-up at 3, 6 and 12 months after treatment and then on a yearly basis. Follow-up consisted of clinical examination, measurement of serum thyroid hormones, serum TSH, serum Tg, anti-thyroglobulin antibodies levels (in group 2) and neck US. A baseline postoperative serum Tg had been checked 6 weeks after surgery.[14] In the absence of detectable serum anti-thyroglobulin antibodies, patients with serum Tg level < 2 ng/dl on and off hormonal therapy were considered disease-free. Conversely, patients with serum thyroglobulin levels > 2 ng/ml, in the presence or not of macroscopically recurrent disease clinically and by investigations, were considered living with disease. ^{131}I WBS was done when indicated.

Data were analyzed by the software IBM-SPSS (version 20). Chi square was done for qualitative data and student *t* test for quantitative data. Survival time was calculated from the time of operation and estimated by using the Kaplan-Meier method. In all tests used, a *P* value is considered significant if it is <0.05 and highly significant if it is <0.001.

RESULTS

This study included 156 patients with low-risk WDTC, of these 28 cases (18%) were males and 128 cases (82%) were females with a female-to-male ratio of 4.6:1 and the mean age was 42.8± 4.12 years.

Of the studied cases, 131 patients (84%) had papillary carcinoma (PTC) and 25 patients (16%) had follicular carcinoma. Pre-operative diagnosis was taken in 93 cases (60%) which was diagnostic in 41 cases (44%). Diagnosis in the rest of cases (115) was made by postoperative histopathologic examination.

A thyroid dysfunction was diagnosed in 31 patients (19.9%); 2 patients (1.3%) had hyperthyroidism and 29 patients (18.6%) had hypothyroidism. Co-existing multinodular goiter (dominant nodule) was present in

69 patients (44.2%) while 87 (55.8%) patients presented with solitary thyroid nodule.

Surgical treatment consisted of TT in 102 patients (65.4%), and HT in 54 patients (34.6%). After surgery 8 patients (7.8%) of TT group developed permanent RLNP, 12 patients (11.8%) developed transient RLNP, 7 patients (6.9%) had permanent hypocalcaemia, and 14 cases (13.7%) had transient hypocalcemia. While in HT group there were no cases of permanent RLNP, 1 case (1.85%) of transient RLNP, 2 cases (3.7%) of transient hypocalcemia and no cases of permanent hypocalcemia. There was a highly significant morbidity rate affecting TT group (*P* value<0.001) (Table 1).

The mean follow-up after first treatment was 8.5 years (ranged from 2-12 years). During Follow-up 25 patients (16%) escaped follow-up 9 patients (5.8%) were in HT group and 16 patients (10.2%) were in TT group. A total of 16 patients (12.2%) of the 131 patients suffered recurrence; of them 9 cases (56.3%) occurred 2-4 years after initial surgery. In the HT group there was a more significant recurrence rate (*P*=0.002) with recurrence in 11 cases (24.4%); of which 7 cases (15.5%) recurred locoregionally (in the thyroid and lymph nodes, 1 case (2.2%) in the contralateral lobe, 1 case (2.2%) in the thyroid remnant and 5 cases (11.1%) recurred within the lymph node basin) and 4 cases (8.9%) recurred in the lung (*P*=0.028). All recurrent cases underwent completion thyroidectomy, MND in those with nodal recurrence and postoperative ^{131}I. In patients underwent TT there were recurrence in 5 cases (5.8%), with 3 cases (3.5%) of clinical recurrence and 2 cases (2.3%) of subclinical recurrence. Of those who recurred clinically 2 cases (2.3%) recurred in the basin of local lymphatics and subjected for MND and one case (1.2%) recurred in the lung which was not responsive to ^{131}I. The cases with subclinical recurrence responded well to ^{131}I. So, there were a total of 13 cases subjected to redo surgery 11 cases of them in the form of completion thyroidectomy in the group underwent HT and 2 cases in the form of MND in the TT group (Table 2).

After redo surgery in TT group one patient (50%) had permanent RLNP, one patient (50%) suffered transient RLNP, and no cases suffered hypocalcemia. While in HT group there was one patient (9.1%) had permanent RLNP, 2 patients (18.2%) suffered transient RLNP, no cases had permanent hypocalcemia, and 2 patients (18.2%) suffered transient hypocalcemia. The morbidity rate was non-significant in-between both groups in the same secession (Table 3).

But strikingly enough to find that the complication rate after completion thyroidectomy in case of HT group is highly significant in relation to the primary surgery (*P*=<0.001) while it was insignificant in the TT group as a whole apart from the RLNP which was significant (Table 4).

All patients who had been treated by TT underwent ^{131}I WBS, and 80 patients (78.4%) of them subsequently received ^{131}I treatment (thyroid remnant in 66 cases 82.5%, and lymph node metastases in 14 cases 17.5%).

In HT group (54 patients), 30 cases (55.5%) developed permanent hypothyroidism requiring administration of L-thyroxine to get TSH suppression.

In TT group, 77 patients (89.5%) were living without disease, 2 patients (2.2%) were living with clinical recurrence in the basin of local lymphatics, 2 patients (2.4%) were living with subclinical recurrence, one patient (1.1%) died with distant metastasis in the lung, and 4 patients (4.6%) were deceased due to causes different from thyroid cancer. At the time of the last follow-up, 81 patients (94.2%) were alive, and 5 (5.8%) had died.

In HT group, 31 patients (68.9%) were living without disease, 9 patients (20%) were living with disease, 4 patients (8.9%) died with distant metastasis in the lung, and 1 patient (2.2%) deceased due to intercurrent diseases. At the time of the last follow-up, 40 patients (88.9%) were alive, and 5 (11.1%) had died (Table 5 & Fig. 1).

Table 1. Operative morbidity according to the technique.

Complication	Patients underwent hemi-thyroidectomy Total=54 (%)	Patients underwent total/ near-total thyroidectomy Total=102 (%)	Chi square	P value
Permanent RLNP	0 (0)	8 (7.8)	4.464	0.035
Transient RLNP	1 (1.85)	12 (11.8)	4.542	0.033
Permanent hypoparathyroidism	0 (0)	7 (6.9)	3.88	0.049
Temporary hypocalcaemia	2 (3.7)	14 (13.7)	3.853	0.05
Total	3 (5.55)	41 (40.2)	20.923	<0.001

Table 2. Effect of extent of thyroidectomy on recurrence (%) at 12 years.

Surgery	Patients	None (%)	Local (%)	Lymph node (%)	Subclinical recurrence (%)	Distant (%)	Overall recurrence (%)
Hemi-thyroidectomy	45	34 (75.6)	2 (4.4)	5 (11.1)	-	4 (8.9)	11 (24.4%)
Total / near-total thyroidectomy	86	81 (94.2)	---	2 (2.3)	2 (2.3)	1 (1.2)	5 (5.8%)
P value	-	-	0.049	0.034	0.3	0.028	0.002
Total patients	131	115	2	7	2	5	16 (12.2%)

Table 3. Rate of complication after redo thyroid surgery in both groups.

Complication	Patients underwent hemi-thyroidectomy (Total=54) No. of recurrences operated (11) (%)	Patients underwent total/near-total thyroidectomy (Total=102) No. of recurrences operated (2) (%)	Chi square	P value
Permanent RLN palsy	1 (9.1)	1 (50)	2.176	0.140
Transient RLN palsy	2 (18.2)	1 (50)	0.965	0.326
Permanent hypoparathyroidism	0 (0)	0 (0)	-	-
Temporary hypocalcaemia	2 (18.2)	0 (0)	0.43	0.512
Total	5 (45.5)	2 (100)	2.026	0.155

Table 4. Rate of complication after first and redo thyroid surgery.

Complication	Patients underwent hemi-thyroidectomy (%)				Patients underwent total/near-total thyroidectomy (%)			
	First surgery	Redo surgery	Chi square	P value	First surgery	Redo surgery	Chi square	P value
Temporary hypocalcaemia	2 (3.7)	2 (18.2)	3.317	0.069	14 (13.7)	0 (0)	0.317	0.573
Permanent hypoparathyroidism	0 (0)	0 (0)	-	-	7 (6.9)	0 (0)	0.147	0.701
Transient RLN palsy	1 (1.85)	2 (18.2)	5.536	0.019	12 (11.8)	1 (50)	2.622	0.105
Permanent RLN palsy	0 (0)	1 (9.1)	4.986	0.026	8 (7.8)	1 (50)	4.410	0.036
Total	3 (5.55)	5 (45.5)	13.479	<0.001	41 (40.2)	2 (100)	2.893	0.089

Table 5. Follow-up.

Outcome	Patients underwent hemi-thyroidectomy (Total=54) No. of Patients (%)	Patients underwent total/near-total thyroidectomy (Total=102) No. of Patients (%)	P
Living without disease	31 (68.9)	77 (89.5)	
Dead of thyroid cancer with distant metastasis	4 (8.9)	1 (1.1)	0.03
Dead of intercurrent disease	1 (2.2)	4 (4.6)	0.485
Alive with disease			
Clinical recurrence	9 (20)	2 (2.2)	0.001
Subclinical recurrence	----	2 (2.2)	0.3
Total	45	86	

*Patients escaped follow-up are 9 patients (16.7%) in the group underwent hemi-thyroidectomy.
*Patients escaped follow-up are 16 patients (15.7%) in the group underwent Total / near-total thyroidectomy.

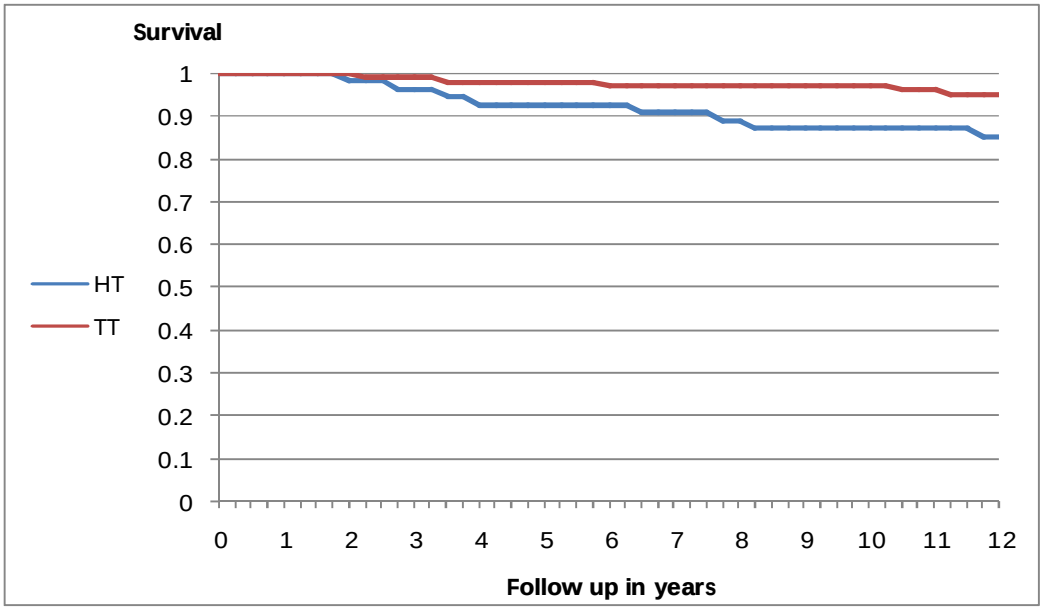

Fig.1 Kaplan Meier plot showing the overall survival rate of both groups through 12 years follow-up. It is clearly shown that TT has a higher survival rate, however, the difference is minimal in the first 3 years, and increases by time after the fourth year.

DISCUSSION

Although thyroid cancer per se constitutes a small percentage among human malignancies, there is a debate among surgeons regarding the extent of surgery especially for the low-risk WDTC due to the relatively dormant course of the disease.

Of the most serious complications after thyroidectomy is permanent hypoparathyroidism which ranges from 5% to 30%.[15] But in experienced hands postoperative hypocalcemia, which is usually transient, occurs in only 6% of patients.[16] In our series, there were greater incidence of temporary hypocalcaemia (13.7: 3.7%) being less in HT group but still the results are comparable to the previous results. While permanent hypoparathyroidism was more significant in TT group (*P*=0.049) although auto-transplantation of one of the

parathyroids is practiced in cases of TT, which decreases the incidence of this complication nearly to zero,[17] which may be explained by the effect of postoperative ^{131}I over the parathyroid glands.

Another feared complication is RLNP which is 1% in experienced hands.[16] In our series, there were greater incidence of RLNP being more in TT group having permanent RLNP in 1.96% (*P*=0.035) and transient RLNP in 3.9% (*P*=0.033). While in HT group there were no permanent RLNP and transient RLNP was 1.85%. These rates come in accordance with the other published studies as complications are reported to increase in patients having more extensive thyroid operations.[18]

Follow-up showed an overall recurrence of 12.2% with a recurrence rate of 24.4% and 5.8% in the group underwent HT and TT respectively after a mean follow-up of 8.5 years, a matter of more than four-fold increase in recurrence rate in HT group as up to 90% of PTC have micrometastatic involvement of the lymph nodes[19] and those patients did not receive postoperative ^{131}I, this comes in accordance with previous report recording recurrence rate of (20% versus 5%) in the group underwent HT and TT respectively.[20] In our series the mean follow-up was 8.5 years and 56.3% of recurrences occurred 2 to 4 years after initial surgery, this comes in accordance with a previous study.[21] We got a significant recurrence rate in HT group in a short follow-up period (*P*=0.002) which may be explained on the basis that this group did not receive postoperative ^{131}I and according to a previous study patients not treated with ^{131}I ablation had a 2.1-fold greater risk of cancer recurrence than those treated with ^{131}I.[22] Most of recurrences in patients underwent HT (64%) occurred locoregionally, this is in accordance with a previous study which may be due to inadequacy of surgery, or underestimation of the patient.[23]

In a previous study recurrence in the contralateral lobe after HT was low 2.7% at 7 years,[24] this encourages doing HT in management of WDTC with its solid indications. In our series recurrence within the contralateral lobe after HT was 2.2%, a lower percentage which may be due to the small number of cases.

In patients underwent HT there were a significant increase in distant metastasis (*P*=0.028), this comes in accordance with data previously reported,[23] this may be due to determination of serum Tg as a postoperative tumor marker is not applicable and distant metastases are often not detected by postoperative ^{131}I scanning because of the presence of a thyroid remnant in those underwent HT.[25]

There was a highly significant morbidity rate incidence in patients experienced completion thyroidectomy than those happened with initial surgery (*P*=<0.001) as completion thyroidectomy is technically more difficult and is associated with increased risk of complications (at least two-fold) due to dissection in scar tissues.[26] The lower incidence of RLNP in the group underwent HT because it is part of the used technique in performing HT not to disturb the strap muscles overlying the healthy side which leaves a virgin plane intact.[27]

L-thyroxine was prescribed post-operatively for life (to TT group and for HT group who developed hypothyroidism) as previous retrospective and prospective studies showed the benefits of TSH suppression in tumor recurrence, progression, and mortality,[28] In contrast, rapid recurrence has been reported after withdrawal of thyroid hormone or administration of recombinant TSH.[29] The results of our study showed that 18.6% of our patients had pre-operative high TSH levels which are associated with higher risk of thyroid cancer in nodular thyroid disease,[30] as TSH is considered as a growth factor for thyroid cancer,[31] in addition 55.5% of HT group developed permanent hypothyroidism depriving conservative thyroidectomy of one of its advantages. A similar observation recorded in a previous study.[32]

There was a significant higher cancer related mortality rate in HT group 8.9% in relation to those underwent TT 1.1% (*P*=0.03). The previous recorded mortality rate for low-risk WDTC is 2-5%.[6]

In conclusion an aggressive three-stage management including TT, ^{131}I ablation and thyroid hormone suppression therapy is warranted for low-risk WDTC.

Limitations: Limitations include the retrospective nature of a highly selected group of patients with WDTC which is not representative of all patients with WDTC. Our findings need to be validated prospectively with a larger population of patients; also patients who had been treated by HT are rather little when compared with those treated by TT.

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