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Total vs hemithyroidectomy for intermediate risk papillary thyroid cancer: A 23 year retrospective study in a tertiary center

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ABSTRACT

Background: There is much debate in the literature over the extent of surgery for patients with intermediate risk papillary thyroid cancer. We herein report our results in a local tertiary hospital.

Method: We identify from our database patients with papillary thyroid cancer who underwent surgery in our hospital and were stratified to be of intermediate risk from the GAMES stratification system. Patients' demographic data, surgical and pathological details were recorded. Primary end points were disease specific survival (DSS) and recurrence free survival (RFS).

Results: From January 1993 to December 2016, 231 patients with papillary thyroid cancer underwent surgery of which 137 (59%) were of intermediate risk. 45 (33%) patients had hemithyroidectomy and 92 (67%) patients had total thyroidectomy. In the total thyroidectomy group, patients had a higher tumor (T) (p value = 0.009) and nodal (N) staging (p value = 0.001). They were also predicted to have a higher risk of recurrence according to the American Thyroid Association (ATA) classification (p value = 0.005). The 5 year DSS in both groups were 100%. The 5 year RFS in the total thyroidectomy and hemithyroidectomy groups were 92% and 100% respectively and were significantly different by the log rank test (p value = 0.02). The median follow up time was 54 months (range 4–276 months).

Conclusion: The 5 year survival in intermediate risk papillary thyroid cancer is favorable. Hemithyroidectomy is an acceptable choice of operation in intermediate risk patients with a better risk profile.

1. Introduction

Thyroid cancer is the commonest endocrine malignancy and is readily treatable and curable in most instances. Its incidence has been rising in recent years across much of the world [1,2]. Various prognostic factors such as age, gender, extent of tumor, size of tumor and presence of distant metastases are well documented prognostic factors [3,4]. Based on clinical and histopathological features, all well differentiated thyroid carcinomas can be classified into low, intermediate and high risk groups based on the GAMES risk stratification system developed by the Memorial Sloan Kettering Cancer Institute in New York [3]. Younger patients below 45 years old, who present with papillary carcinomas smaller than 4 cm in greatest dimension and confined to the thyroid gland are considered at low risk of death. Patients older than 45 years, with extrathyroidal extension, aggressive histological features, disease larger than 4 cm in greatest dimension or distant metastases are at high risk. Traditionally low risk patients are treated by lobectomy and high risk patients are treated by total thyroidectomy. Younger patients with, or older patients without aggressive histological features are considered at intermediate risk. There is still no consensus on the surgical treatment for these patients and this group forms the patient group on which our study is based [4–6].

2. Materials and methods

2.1. Patients

The medical records of 231 patients who underwent surgery at United Christian Hospital from January 1993 to December 2016 were reviewed retrospectively. Patients who met criteria for intermediate risk according to the GAMES classification system were sorted out. All information, including patient characteristics, operative findings, postoperative treatment and follow up, was collected from the patients' electronic medical records. Patients with follicular variant, oxyphilic cell variant, a diffuse sclerosing variant or tall cell variant were excluded. Patients who underwent subtotal thyroidectomy or presented with distant metastases were also excluded from analysis. A total of 137 patients were identified to be of intermediate risk. The median follow

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Table 1
Descriptive statistics of patients.

Variable	Hemithyroidectomy group (N = 44)	Total thyroidectomy group (N = 93)	P value
Sex			
Female	7	59	0.00
Male	37	34	
Age (Mean)	56.7	51.2	0.057
T staging (7th edition)			
T1/T2	40	66	0.009
T3/4	4	27	
N staging (7th edition)			
N0	37	51	0.001
N1	7	41	
Extrathyroidal extension			
No	40	71	0.057
Microscopic	1	17	
Gross	3	5	
[a]ATA grade			
Low	36	49	0.005
Intermediate	3	22	
High	5	21	

[a] ATA- American Thyroid Association.

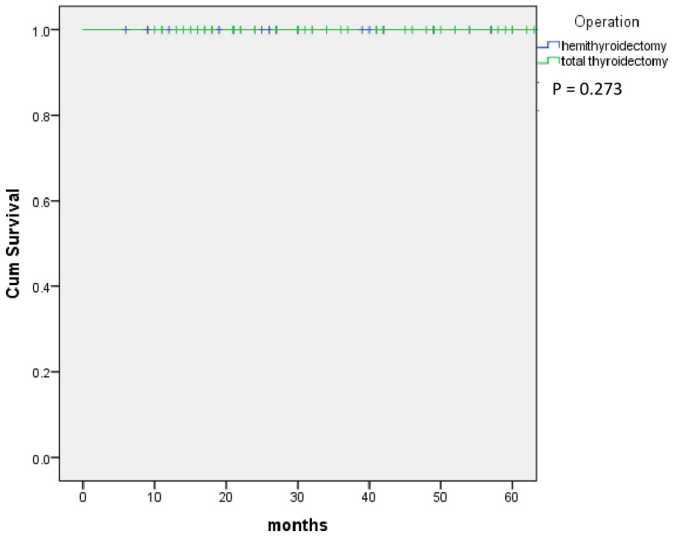

Fig. 1. Survival.

up time was 54 months.

2.2. Surgical strategy

We have long adopted a selective surgical approach for patients with papillary thyroid cancer. When a tumor was restricted to one lobe and there was no evidence of high risk features, which included age > 45 years, cervical lymph node metastases and gross extrathyroidal extension, hemithyroidectomy was performed. Patients with multiple tumors in one lobe were also treated by hemithyroidectomy as long as all tumors were removed. Total thyroidectomy was performed for patients who presented with tumors in both lobes or had high risk features.

Preoperative physical examination and ultrasound was performed by the surgeons. Lateral cervical lymph node dissection (levels II–V) was performed if there was clinical or radiological evidence of lymph node spread. Central compartment lymph node dissection (level VI) was performed for large tumors (> 4 cm) or gross extrathyroidal extension for some of the patients upon discretion by the operating surgeon.

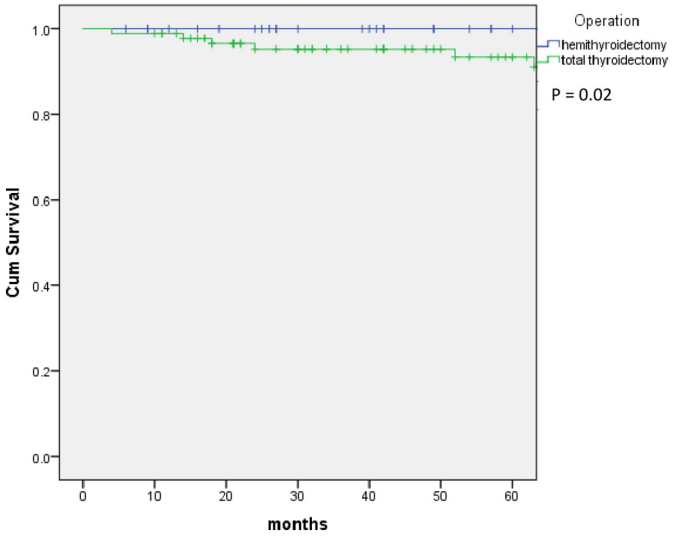

Fig. 2. Recurrence free survival.

Table 2
Risk factors of recurrence.

	P value	HR	95% CI
Age	0.03	1.12	1.01–1.25
Extrathyroidal extension	0.45	2.99	0.18–4.93
T staging (7th edition)	0.03	3.9	1.4–4.7
N staging (7th edition)	0.58	1.75	0.24–12.6
[a]ATA grade	0.8	1.47	0.08–2.75

[a] ATA- American Thyroid Association.

2.3. Statistical analysis

All statistical analysis was performed with SPSS version 22. The disease specific (DSS) and recurrence free survival (RFS) were calculated by the Kaplan-Meier method. Potential risk factors for disease specific mortality or recurrence were subjected to univariate analyses by the log-rank test and to multivariate analyses using the Cox proportional hazard model. The significance level in all of the statistical tests performed in this study was set at $P < 0.05$. The factors that were identified as significant by the univariate and multivariate analyses are reported below with the hazard ratios. The protocol of the present study was reviewed and approved by our Institution's Ethics Board (Ref: REC(KC/KE)-18-0061/ER-4), and the study was conducted in accordance with the Declaration of Helsinki.

3. Results

3.1. Patient characteristics

From January 1993 to December 2016, 231 patients with papillary thyroid cancer underwent surgery at our institution of which 137 (59%) were of intermediate risk. 45 (33%) patients had hemithyroidectomy and 92 (67%) patients had total thyroidectomy. The patients' demographic and tumor characteristics are shown in Table 1. There were 71 male (52%) and 66 female patients (48%). Age ranged from 15 to 80 years and the median and mean age was 53 years.

In the total thyroidectomy group, patients were younger (51.2 vs 56.7 years, p value = 0.057), and had a higher tumor (T) (p value = 0.009) and nodal (N) (p value = 0.001) staging according to the AJCC 7th Edition. The tumors were more likely to have extrathyroidal extension (p value = 0.057). They were also predicted to have a higher risk of recurrence according to the American Thyroid Association (ATA) classification (p value = 0.005).

Table 3
Complication rates.

	Hemithyroidectomy Group (N = 44)	Total thyroidectomy Group (N = 93)	P value
Overall complications	3 (6.8%)	32 (34.4%)	0.001
Transient/permanent vocal cord palsy	2/0 (4.5%/0%)	2/2 (2.2%/2.2%)	0.47
Transient/permanent hypoparathroidism	0/0 (0%)	25/4 (26.9%/4.3%)	0.00
Neck hematoma/seroma	1 (2.3%)	2 (2.2%)	0.96
Wound infection	0 (0%)	0 (0%)	N/A
Reoperation	0 (0%)	4 (4.4%)	0.16

With a median follow up of 54 months, the 5 year DSS in both groups was 100% (Fig. 1). The 5 year RFS in the total thyroidectomy and hemithyroidectomy groups were 92% and 100% respectively and were significantly different by the log rank test (p value = 0.02) (Fig. 2). Within the 5 year postoperative period, there were 7 cases (7.6%) of recurrence in the total thyroidectomy group while none was observed in the hemithyroidectomy group. Using multivariate analyses with Cox regression, a higher tumor staging (hazard ratio = 3.9, p value = 0.03) and age (hazard ratio = 1.12, p value = 0.03) were identified as predictors of higher recurrence. (Table 2).

The complication rates in both groups were listed in Table 3. Vocal cord palsy was defined as transient within 6 months postoperatively and permanent if it persisted beyond 6 months and confirmed on laryngoscopy. Hypoparathyroidism was defined as hypocalcaemia with a low parathyroid hormone level and it was defined as transient within 6 months postoperatively and permanent if it persisted beyond 6 months. There was a significantly higher complication rate in the total thyroidectomy group (p value = 0.001). 34.3% of patients experienced postoperative complications as opposed to 6.8% in the hemithyroidectomy group. 4 (4.4%) patients required reoperation for lateral neck node recurrence. However, excluding hypocalcaemia, there was no significant difference in other complications (4.3 vs 4.4%, p value = 0.98). Among 93 total thyroidectomy patients, 25 (26.9%) had transient and 4 (4.3%) had permanent hypocalcaemia while it is expected that no patient would suffer from hypocalcaemia after hemithyroidectomy.

4. Discussion

A variety of risk stratification systems are available for clinicians for papillary thyroid cancers [7]. At our institution, treatment decisions over the last 20 years have been based on the GAMES classification system. Based on these risk categories, investigators were able to show significant differences in the survival rates [8]. Shaha first proposed the existence of an intermediate risk group with difference in prognosis and survival [3]. The long term survival in low, intermediate and high risk groups was reported to be 99, 87 and 57% respectively [4,5]. Traditionally low risk patients are treated by lobectomy as the long term outcome for PTC patients treated by lobectomy without radioactive iodine is excellent [9–11]. We previously reviewed the results of our own patients with differentiated thyroid carcinoma treated by lobectomy over 24 years and the results were excellent. No patient succumbed to the disease and only 1 out of 93 patients (1.1%) had local tumor recurrence [12]. However, there is general agreement regarding the need for total thyroidectomy in high risk patients. This approach maximizes local control and greatly facilitates treatment of distant metastases with radioactive iodine [13]. However, the extent of surgical resection for intermediate risk cases is still a controversial issue [4–6].

In this study, we demonstrated that in the hemithyroidectomy group, the 5 year DSS was similar and RFS was even better than the total thyroidectomy group. However like all retrospective studies, our data is prone to selection bias. Moreover, the two groups were not completely comparable in that patients who underwent total thyroidectomy had a worse tumor and nodal staging, thus rendering it prone to an inferior outcome. The median follow up time was only 54 months, so limiting the conclusions that can be drawn from the survival data, as recurrences and deaths can occur beyond this time.

Age and Tumor (T) staging were found to be significant prognostic factors of recurrence. It would be difficult to compare for the factors of disease specific mortality in our series since the 5 year DSS approached 100% in both groups. T staging takes into consideration the size of tumor and the presence of extrathyroidal extension. This is line with the multiple risk stratification systems, such as AMES, AGES, MACIS, GAMES, TNM, that have included them as prognostic factors [14]. With the publishing of the 8th edition of the AJCC/TNM cancer staging system, there will be downstaging of a significant number of patients into lower stages, reflecting their low risk of cancer related death. The main changes include a rise in the age cut-off from 45 to 55 years and the removal of lymph node metastases from the Stage III definition. Moreover, microscopic extrathyroidal extension is no longer considered for staging [2]. When implemented, this will entail significant restaging of a lot of our patients and this will require further studies on the predictability of survival as compared to the old system.

As we have shown, patients undergoing lobectomy had fewer complications. There is no risk of hypoparathyroidism while this occurred transiently in 26.9% and permanently in 4.3% of our total thyroidectomy patients. Although we cannot conclude from this study that we should advocate hemithyroidectomy for all intermediate risk patients, we would recommend an individualized approach. A consideration of patient and tumor related prognostic factors and risk stratification are essential steps in the selection of the optimal surgical strategy [13,15]. Given that the survival rate is generally favorable, perhaps it would be reasonable to recommend more conservative surgery in the intermediate- low risk group: intermediate risk patients with a lower tumor or nodal staging.

Disclosure statement

Declaration of interest: none.

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