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SURGICAL STRATEGIES FOR SINGLE-LOBE PAPILLARY THYROID CARCINOMA

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ABSTRACT

Objective: The surgical strategies or range of operation rely on a few specific conditions in the one-sided papillary thyroid cancer, like the size of the tumor, the age of the patient, the invasion of the thyroid capsule by cancer, and the records of blood relatives of thyroid cancer. The study aims to determine the optimal surgical approach for one-sided papillary thyroid carcinoma to maximize patient benefit. Methods: A prospective study of 120 cases in the Comilla Medical College (https://www.cumc.edu.bd) and Comilla Medical Centre, Bangladesh (http://www.comillamedicalcentre.com), from 01 January 2011 to 30 June 2021. Total thyroidectomy (T.T.) + Radioactive Iodine Ablation (RAI) was 70, and hemithyroidectomy (H.T.) was 50; among them, 14 (11.67%) cases relapsed, of which 7 (10%) in the T.T. group and 7 (14%) in the H.T. group, with a mean follow-up of 98.60 months (about 8.25 years). During this period, the overall survival (OS) rate is 100%, and the disease-free survival (DFS) time is 8.9 years in the T.T. group and 8 years in the H.T. group. Results: Tumor size was 50% ≥4 cm and 50% was <4 cm. Females (90.8%), rural residents (71.7%), and people from the lower-middle class (76.7%) were more affected than males, suburban residents, and upper-middle- and higher-class people. Family history of the same disease (85%) and capsular invasion (77.5%) were absent in the maximum cases. Primary surgery was a total thyroidectomy and Radioactive Iodine Ablation (RAI) in 58.3% of cases, and relapsing cases accounted for 11.67%. One-Sample proportions test of both group TT and HT shows a highly notable result that p <001<.05. T-test for self-determining model for GHQ-total for females and males presented analytically meaningful in T.T. that P=.032<.05 and unimportant in H.T. that P=.655>.05. T-test for the self-determining model of the patient's follow-up after surgery between females and males disclosed no substantial variation in T.T. (P=.403>.05) and H.T. (P=.588> .05).05, concluding more negligible in H.T. The association of Pearson relation between age and mindfulness anxiety of MASS total in T.T. was notable, P = .018 <.05, insignificant in H.T. P=.231>.05. The evaluation of multivariate scrutiny among recurrent patient treatment with the anxiety of the patient and check-up time demonstrated extremely significant in TT Pillai's Trace=<.001<.05, mildly adequate in HT Pillai's Trace = .025 < .05. The logistic regression was carried out in SPSS to estimate the odds ratio. The adjusted 95% C.I. for the odds ratio for two groups across significantly different variables: age in years (P = .012 < .05), thyroid capsular invasion (P <.001<.05 in H.T., and sex of the participant (P = .008 <.05, and thyroid capsular invasion P=.042<.05 in TT. Cox regression analysis of different variables to see the hazard ratio, where time is the follow-up of the patient after primary surgery: size of tumor, p =.033, HR=6.845: 95% CI;1.167-40.149, age in years, p=.043, HR=1.082: 95% CI; 1.003-1.167 in the T.T. group, and size of the tumor, p=.993, HR=6406695.899: 95% CI; .000-…, age in years, p=.305, HR=1.083: 95% CI; .930-1.262 in the H.T. group. Conclusion: The study demonstrated that T.T. was more analytically significant and

more convenient than H.T. in single-lobe papillary carcinoma. In logistic regression, age and encroachment of the thyroid capsule by the tumor manifested an important alliance with the outcome of surgery in H.T., and sex and encroachment of the thyroid capsule by the tumor in T.T. In Cog regression survival analysis, tumor size and age were notably associated with survival and recurrence rates in the T.T., whereas no variables were notable in H.T.

KEYWORDS: Hemithyroidectomy (H.T.), Total Thyroidectomy (T.T.), Single Lobe Papillary Thyroid Carcinoma (SLPTC), Radioactive Iodine Ablation (RAI).

1. INTRODUCTION

The prognosis of differentiated thyroid cancer (DTC) is outstanding. Sufferers with stage 1-4 disease have a 10-year survival rate of over 98% [1]. The American Thyroid Association has advocated for more evidence-based treatment and follow-up over the past decade [2]. Thyroidectomy is the mainstay of therapy for thyroid carcinoma. In DTC, a more conservative hemithyroidectomy rather than total thyroidectomy is considered, except in cases with tumor size >4 cm, older age (>55 years), familial history, extrathyroidal spread, multifocal bilateral disease, confirmed nodal or distant metastasis, and potential difficulties with follow-up [3]. It is contradictory that T.T., rather than an H.T., for patients with minimal-risk papillary (PTC) cancer <4 cm in size, has no poor prognosis [4]. Overall, the risk-benefit of H.T. and T.T. for the patient is similar. At the same time, T.T. has a decreased risk of recurrence, long-term follow-up is more cost-effective, and the difference between T.T. and conservative surgery is slight [5]. Papillary thyroid microcarcinoma (PTMC), whose size is less than 1cm, may be found incidentally during frozen section biopsy, after postoperative histopathology, preoperative FNAC, or radiologically. H.T. is associated with excellent survival rates but may have a slightly higher risk of recurrence compared to T.T. [6]. H.T. definitely reduces the hazard of everlasting hypocalcemia and recurrent laryngeal nerve palsy compared to T.T. (7). It reduces the need for lifelong thyroxine replacement (8). There is no notable variation in overall survival (OS) or disease-specific survival (DSS) between patients with low-risk papillary thyroid carcinoma who undergo H.T. and those who have a T.T. (7, 8). Some studies report that T.T. has a better recurrence-free survival rate ($p<.001$), though the absolute difference is often observed in low-risk patients (9). Prophylactic neck dissection is not recommended unless the patient is otherwise high-risk, with a tumor size >4 cm, or extrathyroidal extension, as it supplies a better outcome [10]. Radioiodine ablation (RAI) destroys residual thyroid tissue, and micro-metastatic lymph node ablation with 131I, called radiation remnant ablation (RRA), reduces locoregional recurrence and increases survival [11]. For effective RAI ablation, T.T. and neck dissection are required for neck node metastasis, and patients who have previously undergone H.T. require a completion thyroidectomy [12]. In 2009, the American Thyroid Association (ATA) recognized the importance of stratifying risk into low, intermediate, and high for recurrence prediction [13]. Follow-up should be maintained for up to 10 years by the primary surgeon and the nuclear medicine department, and lifelong by the thyroid clinic. Keep the tumor marker Tg (Thyroglobulin) level < 1 mcg/L, Neck U.S. negative, and TSH 0.3-2.0 mU/L to prevent recurrence [14]. Relapse cases may present with recurrence in the thyroid bed or surrounding structures, locoregional lymph nodes, and distant metastasis, which are treated both surgically and with RAI ablation [15] [16].

Figure 1: Right-sided SLPTC of a woman

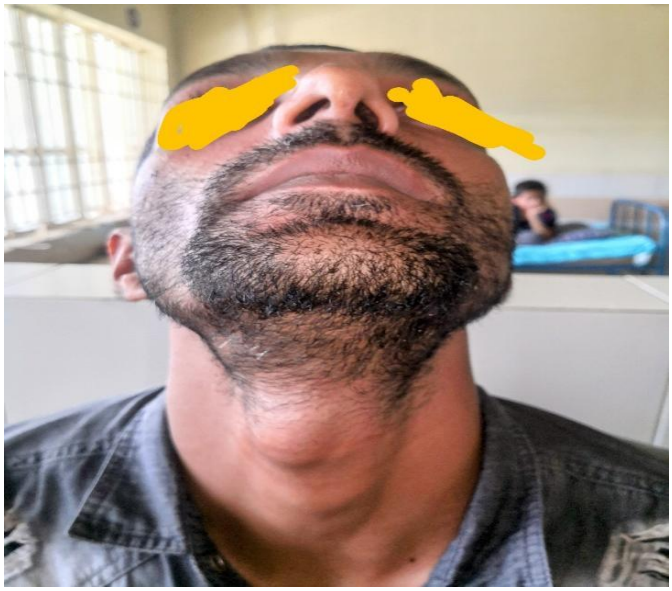

Figure 2: Right-sided SLPTC of a man

Figure 3: Left-sided SLPTC of a woman

Figure 1: Right-sided SLPTC of a woman

2. METHODS:

2.1. Experimentation Outline:

It is a comparative study conducted in two tertiary care hospitals from 01 January 2011 to 30 June 2021. During this time, the AJCC (American Joint Committee on Cancer) published TNM staging, with the seventh edition in January 2010 and the eighth edition in October 2016. So, I follow the staging, treatment, and follow-up accordingly. So, some patients' surgeries depend on the seventh edition, and others on the eighth edition. One hundred twenty euthyroid single lobe papillary thyroid carcinoma patients' demographic data, diagnosis, operations, outcome, follow-up, and relapse case management details were written accordingly. All patients are clinically diagnosed as euthyroid and established by patients' records, check-up, and fundamental inquiries, including thyroid function tests, serum calcitonin, USG of the Thyroid gland and neck, FNAC, FOL, CT scan, and MRI, as needed. My categorical variables are tumor size, sex, residential status, socioeconomic condition, family history, capsular tumor invasion, types of surgery, outcome, and relapse case management, and continuous variables are age in years, GHQ about thyroid disease, Mindfulness anxiety questionnaire, follow-up with the patient after surgery, and recurrence of disease after primary surgery in months. I scrutinize all data in SPSS category 31.

2.2. Interventional Plan:

Primarily, we have to follow two interventional procedures according to the ATA 7th and 8th guidelines: total thyroidectomy (T.T., N-70) and hemithyroidectomy, which includes the affected lobe and isthmus (H.T., N-50). The surgical procedure was fully explained to the patient. The pros and cons of both surgeries were elucidated to the patient and their relatives. The thyroid hormones are essential for energy metabolism, heat production, brain development, bone growth, blood flow, and mood, reflexes, and mental sharpness. Total thyroidectomy (T.T.) needs lifelong replacement therapy of thyroid hormone and some irreversible complications, with a lower recurrence rate. Hemithyroidectomy (H.T.) preserves hormone function, which is more important for women's reproductive life. It has fewer complications but a slightly higher recurrence rate than T.T. It is most important to preserve the most essential gland to maintain a young patient's conjugal life.

2.3. Follow-up schedule and consequences:

A strict follow-up was advised for both high and low-risk patients. During follow-up, the sufferers' investigations included ultrasonography (USG) of the neck and thyroid gland, and serum Tg, FT4, and TSH for the T.T. group, and USG of the neck and thyroid gland, and serum FT4 and TSH for the H.T. group. Every six months for five years and every year for the following days. Some high-risk patients have elevated TG after treatment with T.T. and radioactive iodine ablation, but a PET-CT (Positron Emission Tomography-Computed Tomography) scan shows no abnormality. So, the follow-up is most important for a disease-free life. One patient included in our research, after the first surgery of total thyroidectomy and radioiodine ablation, presented lymph node metastasis, and the patient was managed by neck dissection and a second radioiodine ablation. The patient relapsed after 14 years after the first surgery, showed a continuous increase in Tg, and US showed a small mass that increased in size over the next 3 years. After PET-CT, the precise location of the mass was identified, and the decision was made to perform the third surgical procedure. During surgery, a persistent disease was shown at the site of the nerve, which failed to track during the primary and second surgeries. After surgery, Tg drops to less than 0.01 mcg/L, down from a previous high of 30 mcg/L.

2.4. Hypothesis and Statistical analysis:

In illustrative statistics, I examine expressive variables by occurrence and proportion, and assessable variables by mean, median, mode, and standard deviation. deviation. After assessing the study's validity, I used inferential statistics, including significance tests, to either accept or reject the null hypothesis. Chi-Square test for non-numerical variables, and t-test for numerical variables. Firstly, the Chi-Square test on the expressive variables in both the T.T. and H.T. groups. Secondly, a one-sample t-test for each variable in the T.T. and H.T. groups. I conducted a t-test for the self-determining model (a parametric test) on GHQ total scores for females and males in both groups, T.T. and H.T. I also conducted an Independent Samples t-test on patients to assess any differences in follow-up after surgery between males and females in both groups. The Pearson test was used to assess the correlation between age and Mindfulness anxiety within the two groups. The evaluation of multivariate scrutiny among recurrent patient treatment with the anxiety of the patient and check-up time. Multivariate analysis, or a one-way MANOVA, showed that follow-up time moderates the relationship between case management, mindfulness, anxiety awareness, and relapse in both categories. Logistic regression was performed for both TT and HT to estimate odds ratios. The dependent variable was the outcome of primary surgery, with other variables including tumor size at primary surgery, sex, age in years, family history of the same disease, tumor capsular invasion, patient follow-up after surgery in months, and recurrence of disease after primary surgery in months. I adjust the importance level to $P < .05$ (two-tailed).

3. RESULTS:

3.1. Participant features according to intervention:

The patient's records, clinical outcomes, and investigations are the momentous factors in determining whether to perform a total thyroidectomy (T.T.) or a hemithyroidectomy (H.T.). Tumor size is the main factor in determining the surgical procedure, whether T.T. or H.T. Here, tumor size ≥4cm, 55(78.57%) in the T.T. and 5(10%) in the H.T. group, tumor size <4cm, 15(21.43%) in the T.T. and 45(90%) in the H.T. group. The other factor, age, is also a concern in the ATA guideline in the 7th and 8th editions. The mean age and Std. deviation in the T.T. was 41.07±11.099, in the H.T. 30.50±8.074 years. The patient's age risk is over 45 years according to the 7th ATA guideline and 55 years according to the 8th, so we need to minimize both factors when selecting an appropriate surgical procedure. Family history of papillary thyroid carcinoma was a critical part of the surgical intervention. Family history of thyroid cancer was present in 9 (12.9%) in the T.T. group and in 9 (18%) in the H.T. group, with equal rates in both groups. Here, the family history of papillary carcinoma was more advanced in the H.T. group (18%) than in the T.T. group (12.9%). This reflection was a more conservative surgery, which was unusual. Capsular invasion of the carcinoma was present in the T.T. group, 20(28.6%), and 7 (14%) in the H.T. group. This was authentic for extensive surgery. Socioeconomic and residential status both had a high rate of poor (54; 77.1%) and rural (50; 71.4%) in the T.T. group, and poor (38; 76%) and rural (36; 76%) in the H.T. group. This is an actual scenario in the developing countries where poor and rural people have the choice of surgery, which is controversial in a sense that they are dependent on the government hospital. They have to wait a long period to be admitted to the hospital, and after admission, the date of surgery also takes one to two months.

3.2. Relapsing and survival:

The overall (OS) survival rate was 100%, and disease-free survival (DFS) time was 8.9 years in the T.T. group and 8 years in the H.T. group. Only one patient included in our study after hemithyroidectomy had a third recurrence due to persistent microtissue, with radioactive iodine ablation not working; the tumor gradually increased in size and was diagnosed during follow-up, with persistently rising serum Tg and US showing a size of 0.2 mm to 1.4 cm after 8.5 years following the second surgery. The patient had been included in our survey after the first surgery. Figure 1-4 shows the single-lobed papillary carcinoma in four female and male patients. Expressed statistics are presented for unequivocal variables as frequencies and percentages for both the T.T. and H.T. (Table 1), and for assessable variables as mean, median, mode, and S.D. for both the T.T. and H.T. groups (Table 2). In the crosstab, we estimate the risk. The chi-square test showed that the P-values and odds ratios for the different expressive variables, including tumor size and family history of papillary carcinoma, were p value=.071 (> 0.05) and odds ratio value for tumor size=3.639; family history, absent=1.240, and present=.341 in the T.T. group, and p value=.269, odds ratio value for tumor size=00, family history, absent=1.250 in the H.T. group, thyroid capsular invasion and outcome of surgery, p value=.008, odds ratio value for capsular invasion=8.00, outcome of surgery, cure=1.280, relapse=.160 in the T.T., and, capsular invasion p value=<.001; odds ratio for capsular invasion = 17.778, outcome of surgery, cure=2.171, relapse=.122 in the H.T., sex of the patient, and outcome of surgery, p value=<.001, odds ratio for sex=15.000, outcome of surgery, cure=1.875, relapse=.125 in the T.T. group, and p value=.689, odds ratio for sex=1.625, outcome of surgery, cure=1.083, relapse=.667 in the H.T. group(Table 3). A One-Sample t-test was performed for all expressive and assessable variables in both the T.T. and H.T. groups, yielding a highly significant result (p < .001).05 (Table 4). In the Independent-Samples t-test, my hypothesis is: A. Invalid (H0): There is dissimilarity in the mean GHQ outcome between males and females. B. Possible (H1): There is a significant difference between male and female scores. My results showed significance in T.T. (Two-Sided P = .032 < .05) and rejected the null hypothesis; H.T. was insignificant (Two-Sided P = .588 > .05), and I did not reject the null hypothesis. T-test for the self-determining model of the patient's follow-up after surgery between females and males disclosed no substantial variation in T.T. (P=.403>.05) and H.T. (P=.588> .05).05, concluding more negligible in H.T. I accept the null hypothesis that there is no potential difference in follow-up after surgery between males and females. Pearson's Correlation between age and Mindfulness anxiety in T.T. showed a significant relationship (2-tailed P = .018 < .05). In contrast, in H.T., it was insignificant (2-tailed P = .231 > .05). Multivariate analysis (MANOVA) showed an interaction effect of relapse case management on follow-up time and Mindfulness anxiety in patients. I hypothesised that: A. Null (H1): There is no significant interaction effect of relapse case management with follow-up time and Mindfulness anxiety. B. Alternate (H1): There is a significant interaction effect of relapse case management with follow-up time and Mindfulness anxiety. The test results showed a highly significant result in TT Pillai's Trace (p <.001 <.05) and a mildly significant result in HT Pillai's Trace (p = .025 <).05 (Table 5), which is less

significant than T.T. In the binary logistic regression, the adjusted 95% CIs for the odds ratio (Exp(B)) for the tumor size during primary surgery: p = .625>05, lower bound = -.225, upper bound =.139, sex of the participant, p = .006 < .05, lower bound = .106, upper bound =.593, age in years, p=.244>.05, lower bound= -.003- upper bound=.013, thyroid capsular invasion of carcinoma, p=.032<.05, lower bound= .015- upper bound= .305 in the T.T. group, and the tumor size during surgery: p=.246>.05, lower bound= -.154-upper bound=.547, sex of the participant: p=.830>.05, lower bound=-.257-upper bound=.319, age in years: p=.029<.05, lower bound =.002-upper bound=.027, thyroid capsular invasion of carcinoma, p= <.001<.05, lower bound = .235, upper bound = .759 in the H.T. group (Table 6). Cox regression analysis of different variables to see the hazard ratio, where time is the follow-up of the patient after primary surgery: size of tumor, p =.033, HR=6.845: 95% CI;1.167-40.149, age in years, p=.043, HR=1.082: 95% CI; 1.003-1.167, capsular invasion, p =.248, HR=2.267: 95% CI;.588-9.092, family history, p=.749, HR=1.499: 95% CI; .149-14.059 in the T.T. group, and size of the tumor, p=.993, HR=6406695.899: 95% CI; .000-…, age in years, p=.305, HR=1.083: 95% CI; .930-1.262, thyroid capsular invasion, p=.357, HR=3.228: 95% CI; .267-39.087, and family history of carcinoma thyroid, p=.478, HR=2.407: 95% CI; .213-27.271 in the H.T. group (Table 7).

3.3. Possible danger for relapse following carcinoma of the thyroid surgery:

Tumor size, age, capsular invasion, and family history are potential risk factors for relapse in papillary carcinoma. The Chi-Square test showed the odds ratios for tumor size (3.639), family history (absent, 1.240), and absence (0.341) in the T.T. group. The odds ratio of tumor size=0, family history absents=1.250 in the H.T. group, and the p-value is nonsignificant in both groups. However, the odds ratio values in both variables are above 1, which indicates that tumor size and family history were a danger for relapse of the disease. The odds ratio for thyroid capsular invasion is 8.00, and the surgical outcomes are cure (1.280) and relapse.160, p value = .008; also significant in the T.T., and odds ratio for capsular invasion = 17.778; outcome of surgery: cure = 2.171, relapse = .122, and p value = <.001 in the H.T. So, capsular invasion was another risk factor both for T.T. and H.T. Here, another risk factor is the patient's sex, with an odds ratio of 15.000 in T.T. and 1.625 in H.T.

In the logistic regression, sex and capsular invasion were both significant risk factors in T.T., with p-values of .006 and .032, respectively, and age and capsular invasion were significant in H.T., with p-values of .029 and <.001, respectively. Cox regression analysis indicated that tumor size was a probable dangerous factor (p = .033, HR = 6.845) and age (p =.).043, HR=1.082 in T.T. and insignificant in H.T., where the size of the tumor, p=.993, HR=6406695.889, and age in years, p=.305, HR=1.083. In the multivariate analysis, relapse case management showed significant results in both T.T. and H.T., with p-values of <.001 and .025, respectively. The surgical management of relapse cases included in the second surgery for T.T. included neck dissection for metastatic lymph node and radioactive iodine ablation, and H.T. requires completion thyroidectomy; if metastatic lymph node is present, neck dissection was performed; if not present, central compartmental neck dissection was routinely performed, afterwards radioactive iodine ablation and follow-up.

Table 1: Frequency and Percentage of Categorical Variables in T.T. and H.T.

Factors	Type	TT	N-70	HT	N-50	Total
		Frequency	Percentage	Frequency	Percentage	
Tumor size during surgery	≥4cm	55	78.57%	5	10%	60
	<4cm	15	21.43%	45	90%	60
Sex of the participant	Female	64	91.4%	6	8.6%	70
	Male	45	90%	5	10%	50
Socioeconomic status	Poor	54	77%	38	76%	92
	Lower middle	10	14%	7	14%	17
	Upper middle	6	8.6%	5	10%	11
Residential status	Rural	50	71.4%	36	72%	86
	Suburban	9	12.9%	6	12%	15
	Urban	11	15.7%	8	16%	19
Family history of the same disease	Absent	61	87.1%	41	82%	102
	Present	9	12.9%	9	18%	18
Capsular invasion of carcinoma	Absent	50	71.4%	43	86%	93
	Present	20	28.6%	7	14%	27
Outcome of primary surgery	Cure	63	90%	43	86%	106
	Relapse	7	10%	7	14%	14
Relapse case management	No relapse	63	90%	43	86%	106
	Neck dissection, RAI	7	10%			7
	Completion thyroidectomy, Neck dissection, RAI			7	14%	7

Table 2: Mean, Median, Mode, SD, and Range of Continuous Variables in T.T. and H.T.

Factors	TT					HT				
	Age in years	GHQ	MAAS	Follow up in the month	Recurrence after primary surgery in months	Age in years	GHQ	MAAS	Follow up in the month	Recurrence after primary surgery in months
Mean	41.07	23.64	30.73	100.20	107.43	31.50	23.68	30.72	96.36	96.00
Median	41.00	23.00	30.50	102.20	130.00	30.50	23.00	30.00	99.00	94.00
Mode	38	25	26	132	130	30	25	26	120	65
Std. Deviation	11.099	4.239	4.208	23.679	28.988	8.074	8.074	4.779	4.558	20.785

Table 3: Risk Estimate with odds ratio for patients with different expressive variables in the chi-Square test, both in T.T. and H.T.

Factors		TT		95% confidence	interval	HT			95% confidence	interval
	P value	Odds ratio	value	lower	upper	P value	Odds ratio	value	lower	upper
Size of tumor: Family history	.071	Size of tumor	3.636	.838	15.782	.269	Size of tumor	00	00	00
		Family history: Absent	1.240	.903	1.701		Family history: Absent	1.250	1.080	1.447
		Present	.341	.104	1.114		present	00	00	00
Thyroid capsular invasion: Outcome of surgery	.008	Capsular invasion	8.00	1.405	45.545	<.001	Capsular invasion	17.771	2.656	119.093
		Outcome of surgery: cure	1.280	.988	1.659		Outcome of surgery: cure	2.171	.919	5.126
		Relapse	.160	.034	.758		Relapse	.172	.034	.433
Sex of the patient: Outcome of Surgery	<.001	Sex	15.000	2.258	99.639	.684	Sex	1.625	.154	17.105
		Outcome: Cure	1.875	.840	4.184		Outcome: Cure	1.083	.689	1.704
		Relapse	.125	.036	.432		Relapse	.667	.099	4.478

Table 4: One-Sample t-test of different variables.

Factors	TT	N-70		HT	N-50	
	t	df	P Value	t	df	P Value
Size of the tumor during surgery	24.589	69	<.001	44.333	49	<.001
Sex of the participant	32.216	69	<.001	25.667	49	<.001
Age in years	30.959	69	<.001	27.586	49	<.001
Family history of the same disease	28.007	69	<.001	21.500	49	<.001
Thyroid capsular invasion of carcinoma	23.641	69	<.001	22.998	49	<.001
Outcome of primary surgery	30.458	69	<.001	22.998	49	<.001
Relapse cases management	30.458	69	<.001	12.911	49	<.001
GHQ about thyroid disease	46.661	69	<.001	35.041	49	<.001
MAAS	61.095	69	<.001	47.656	49	<.001
Follow up with the patient after surgery in months	35.404	69	<.001	30.738	49	<.001
Recurrence of disease after primary surgery in months	9.805	6	<.001	12.220	6	<.001

Table 5: Multivariate Tests of the interaction effect of relapse case management on follow-up and mindfulness anxiety in T.T. and H.T.

Factors		TT	N-70	HT	N-50
		F	P Value	F	P Value
Relapse management	Pillai's Trace	8.761	<.001	3.990	.025

Table 6: Binary logistic regression of different variables in TT and HT, where the dependent variable is the outcome of primary surgery.

Factor	TT		95% confidence	interval	HT		95% Confidence	interval
	t	P value	Lower bound	Upper bound	t	P value	Lower bound	Upper bound
Size of tumor	-.492	.625	-.228	.138	1.131	.264	-.154	.547
Sex	2.868	.006	.106	.593	.216	.830	-.257	.319
Age	1.175	.244	-.003	.013	2.256	.029	.002	.027
Capsular invasion	2.197	.032	.015	.305	4.026	<.001	.253	.759

Table 7: Cog regression analysis of different variables in TT and HT, where the time variable is the follow-up of the patient after primary surgery.

Factor	TT		95% confidence	interval	HT		95% confidence	interval
	P Value	Exp(B)	Lower bound	Upper bound	P Value	Exp(B)	Lower bound	Upper bound
Size of tumor	.033	6.845	1.167	40.149	.993	6406695.899	.000	
Age	.043	1.082	1.003	1.167	.305	1.083	.903	1.262
Capsular invasion	.248	2.267	.566	9.082	.357	3.228	.267	39.087
Family history	.749	1.449	.149	14.059	.478	2.407	.213	27.271

4. DISCUSSION:

The thyroid gland is the body's primary executive endocrine organ, playing a crucial role in regulating numerous bodily functions essential to life and overall health. It influences almost every single cell in the human body. The hormone regulates the body's metabolic, cardiovascular, respiratory, and thermoregulatory functions, growth and development, mental and emotional health, and reproductive function. Well-differentiated thyroid carcinoma, like papillary thyroid carcinoma, is an ideal cancer that presents in various ways. As a benign carcinoma, it has a very satisfactory outcome. Though surgery is the primary treatment, some patients are waiting for a period of time to delay the operation. The surgeon or the patient has different surgical options; which one is appropriate for the patient? The appropriateness of surgery depends on tumor size, sex, age, family history, capsular invasion of carcinoma, and extrathyroidal extension, such as locoregional lymph node metastasis. Sometimes one lobe is affected with papillary carcinoma of the thyroid, with other risk factors like tumor size greater than 4 cm, family history of papillary carcinoma, and capsular invasion of carcinoma. However, the decision was H.T. due to organ preservation, to maintain a normal reproductive life, and to preserve the gland with continuous follow-up. A few patients, like T.T., underwent radioactive iodine ablation after diagnosis of unilateral swelling of papillary carcinoma with replacement therapy of thyroxin for the whole life, and follow-up. The present paper is a comparative study of T.T. and H.T. for SLPTC, a subject that has remained debated in the past, present, and future.

4.1. Size of the Tumor during Primary Surgery:

The unilateral papillary thyroid carcinoma ranged in multiple sizes. Here, we divided the size into two groups: <4 cm (15; 21.43%) in the T.T. group and (45; 90%) in the H.T. group, and ≥4 cm (55; 78.57%) in the T.T. group, (5; 10%) in the H.T. group. Albinsaad L.S. [17] reported results similar to ours: ≤2cm (62; 100%) in the lobectomy group and 104 (76.5%) in the total thyroidectomy group. and >2 cm (32; 23.5 %) in the total thyroidectomy, similar to our study. Huang H. [18] demonstrated that tumor size was ≤2 cm in 71 (57.7%) and >2 cm in 52 (42.3%), findings consistent with our research. Bosset M.'s [19] study examined recurrence and nonrecurrence cases; the mean tumor size for the 295 cases was 22.9 mm; for the 255 (86.44%) nonrecurrence cases, 22.6 mm; and for the 40 (13.56%) recurrence cases, 25 mm. Park K.W.'s [20] work reported 22,383 patients with a tumor mean size of 5.2 mm (subtotal or hemithyroidectomy), 16,475 patients with a tumor mean size of 5.5 mm (subtotal or hemithyroidectomy), and 4,300 patients with a tumor mean size of 4.3 mm (lobectomy). Wu Z.'s [21] paper displayed only total thyroidectomy, and central neck dissection (1001 patients, first group), and total thyroidectomy, central neck dissection, and lateral neck dissection (1107 patients, second group), classified by tumor size centimeter theatrically as follows: T1a≤0.5 cm, 0.5cm<T1b≥1cm, 1cm<T1c≥2cm, 2cm<T2≥5cm, and T3>5cm. First group of patients' T1a was 300(29.97%), T1b 370(36.96%), T1c 235(23.48%), T2 85(8.49%), and T3 11(1.10%), second group of patients' T1a 442(20.97%), T1b 720(34.16%), T1c 604(28.65%), T2 316(14.99%), and T3 26(1.23%). His paper established that the preliminary surgery for papillary thyroid cancer was total thyroidectomy, which was our research decision, and statistically proven. Geron Y's. (8) research paper exhibited that the tumor size was <1cm; 86(81.9%), >1cm; 23(18.01%) in the hemithyroidectomy group, 1-30 mm; 50(100%) in the total thyroidectomy group, which is similar to our study.

4.2. Sex of the Participant:

Here females (90.8%) are more than males (9.2%), supported in the T.T. group, female 64(91.4%); male 6(8.6%), in the H.T. group, female 45 (90%); male 5(10%), supported by Albinsaad L.S. [17] demonstrated that in the lobectomy group, female 54(87.1%); male 8(12.9%), in the T.T. group, female 126(92.6%; male 10(7.4%), very close to our paper. Bosset M. [19] exhibited his long-term outcome of lobectomy for thyroid cancer female was, females were 234 (79.32%), males were 61(20.68%), recurrence -free female females were 205(87.6%), recurrence

29(12.4%), and recurrence -free males were 50(82%), recurrence 11(18%), similar to our research. K.W. Park's [20] paper revealed that the subtotal or total thyroidectomy group's females were 13846(84%), and males 2629(16%); females were 4562(78.5%), and males were 1246 (21.5%) in the lobectomy group. Geron Y. [8] reported that females accounted for 92 (84.4%) and males for 17 (15.6%). Lim H [16] reported that, in the SEER-9 database, females accounted for 75.3% and males for 24for24.7%. H. Huang [18] reported that females accounted for 68.29% and males for 31.71%. Wu Z [21] reported that 80.27% were female and 19.73% males.

4.3. Age of the Patient:

The mean age and SD of the current study were 36.08±10.998 years, with a median of 36.00, ranging from 18 to 61 years; 90 (75%) cases were <45 years, 30 (25%) cases were≥45 years, and 09 (7.5%) cases were≥55 years. The mean age and SD of the T.T. were 41.07±11.099 years, with a median of 41.00, 27(38.57%) cases were≥45 years, 43(61.43%) cases were <45 years, and 09(12.86%) cases were≥55 years, the mean age and SD of the H.T. were 31.50±8.074 years, with a median of 30.50, 03(6%) cases were ≥45 year, 47(94%) cases were >45 years, and no cases were greater than 55 years. Albinsaad L.S. [17] reported that the mean age and SD in the lobectomy group were 46.2±9.2 years, and in the total thyroidectomy group were 45.4±12.4 years, a significant difference from our work. Huang H. [18] confirmed his work only lobectomy, median age was 43 years, ranged from 15-78 years, 74(60.2%) cases were <45 years, 49(39.8%) was ≥45 years near our study while Wu Z [21] paper included 2108 cases age ranged from 13-79 years, 897(42.56%) cases ≤40 years, 619(29.36%) cases ≤ 50, 592(28.08) ≥60 against my work. Bosset M. [19] reported only lobectomy of 295 patients, with a mean age and SD of 39.8±12 years; for nonrecurrence, 255 patients had a mean age and SD of 39.9±11.9 years; and for recurrence, 40 patients had a mean age and SD of 38.9±13.0 years, which is close to our paper. Park K.W. [20] worked with the SEER database (http://www.seer.cancer.com), where the mean age and SD of all patients (22,283) were 51.9±13.9 years, sub-total or total thyroidectomies (16,475) mean age and SD were 51.5±13.8 years, and lobectomies (5805) mean age and SD were 53.0±14.1 years, matching our study. Geron Y. [8] reported baseline characteristics of 109 (68.55%) patients undergoing hemithyroidectomies, with a mean age of 50.1±13.3 years. and of 51.8±16.8 years for total thyroidectomies, comparable with our study. The ATA age cutoff for a high-risk TNM stage increased from>45 years in the 7th edition to >55 years in the 8th edition. Kim M [22] showed that a high-risk cut-off age of >55 years is appropriate in TNM staging to predict disease-specific survival (DSS) in 6333 cases of PTC.

4.4. Socioeconomic and residential status of the Patient:

Considering socioeconomic and residential status, poor and rural people suffer more from SLPTC in our work. Due to greater iodine deficiency in rural areas and a lack of health education among poor people, goiter prevalence is 20% in Bangladesh [23]. Weigle DS showed that 3.95% of Indian people suffer from thyroid disease, similar to Bangladesh [24].

4.5. Family history of Papillary Thyroid Carcinoma:

In the present research, a family history of thyroid carcinoma is present in 9 (12.9%) of the T.T. group, 9 (18%) of the H.T. group, and, overall, 18 (15%) of 120 patients. Dong F [25] reported that ionizing radiation, iodine intake, environmental endocrine disruption, and heredity are risk factors for thyroid cancer, findings reflected in our work. The family history of thyroid cancer was 15% among total patients (120) in our research, supported by Haugen RR [3], who reported that 5-10% of affected carcinomas have a familial history.

4.6. Capsular Invasion of the thyroid carcinoma:

It is not uncommon that a few patients present with capsular invasion or extrathyroidal extension. In our study, overall capsular invasion was 22.5% (27 out of 120), and in the T.T. group, it was 28.6% (20), and in the H.T. 14% (7), similar to Wu Z's [21] finding that 22.91% (483) out of 2108 total patients have a capsular invasion. Albinsaad L.S. [17] reported that capsular invasion or extrathyroidal extension was 24 (38.7%) in the lobectomy group and 79 (58.1%) in the total thyroidectomy group, which is about double the rate in our study. Huang H. [18] studied the long-term outcome of lobectomy for single-lobe papillary thyroid carcinoma; they reported 30 (24.4%) cases with extrathyroidal extension, which is consistent with our paper. Geron Y. [8] reported that the long-term outcome of hemithyroidectomy shows extrathyroidal extension in 7 (6.5%) of 109 patients, which is less than half of our study.

4.7. Primary Surgery and Follow-up the Patient:

In our paper, 58.3% (70) of primary surgeries were T.T. and Radioactive Iodine Ablation, and 41.7% (50) were H.T., in accordance with the ATA guidelines 7th and 8th. The mean and SD of the follow-up time were 120±23.697 months in the T.T. group, 96.36±4.558

months in the H.T. group. Albinsaad L.S. [17] reported that 62 (33.33%) were lobectomies and 124 (66.67%) were total thyroidectomies. The follow-up period for the lobectomy group was 119±48 months, and for the total thyroidectomy group was 127±40 months, which is parallel with our research. Both follow-ups every 6 months near Hui H [17] showed: 66.69% H.T., 27.64% HT+ contralateral Lobectomy, 5.69% HT+ subtotal lobectomy with neck dissection, among them, central compartmental neck dissection did 67 cases, with lateral neck dissection of 3 cases, lateral neck dissection did 39 cases, no RAI, and follow-up with levothyroxine. The mean follow-up was 98.60 months (about eight years), median 102.00, ranging from 60-132 months (about 11 years) in our work, consistent with Huang H's [18] study, which reported a median follow-up of 96 months (about eight years) and ranged from 12-157 months (about 13 years) which was more than our reports. Bosset M. [19] showed that all their primary surgeries were lobectomies and total thyroidectomies in accordance with the 8th ATA guideline; lobectomy was 91.1% (261) in the low-risk group: tumor size ≤4 cm, and total thyroidectomy was 24 (8.1%) in the intermediate-risk group: tumor size >4 cm. After 10 years of follow-up, disease-free survival cases were 255 (86.44%) and recurrence cases were 40 (13.6%), consistent with our study. Park K.W. [20] reported that 16,475 patients underwent total thyroidectomy (73.9%) and 5,805 lobectomy (26.1%), findings similar to ours. They follow up with the patient and use Kaplan-Meier survival analysis; the PTMC patient showed similar OS between lobectomy (5.8 years) and total thyroidectomy (5.82 years), consistent with our study: H.T. was 8.25 years, and T.T. was 8.9 years. Wu Z. [21] reported surgery for 1001 (47.48%) patients with total thyroidectomies and central lymph node dissection, and 1107 (52.51%) patients with total thyroidectomies, central lymph node dissection, and lateral neck node dissection, which was applied in our relapsing cases with neck node metastasis. Geron Y. [8] performed hemithyroidectomies in 109 (68.55%) patients and total thyroidectomies in 50 (31.45%) patients, which is close to our research. They maintain the follow-up 8.6 years of 109 hemithyroidectomy patients with DFS of 98 patients (89.91%), and recurrent case was 11(10.09%), 7.1 years of 50 total thyroidectomies patients with DFS 49 (98%), and recurrent case was 01(2%), also close to our study.

4.8. Management of Relapsing cases:

During follow-up, 10% (7) relapsed in T.T., and 14% (7) in H.T. The total across 120 patients was 11.67% (14), and the disease-specific survival rate was 100%. The relapsing cases of T.T. were presented with metastasis to the lateral cervical neck node in 03 (42.86%) patients and to the central neck node in another 04 (57.04%) patients. They are managed with neck dissection; lateral and central neck node dissection of both groups following radioactive iodine ablation. In the H.T. group, 05 (71.43%) presented with papillary carcinoma in the contralateral lobe, and the remaining 02 (28.57%) presented with papillary carcinoma in the contralateral lobe and metastasis to the lateral neck node. This group managed with the completion of thyroidectomy and central and lateral neck node dissection following radioactive iodine ablation. All relapsed patients were advised on replacement therapy, levothyroxine, and lifelong follow-up. Albinsaad L.S. [17] reported overall recurrence was 24 (12.12%), type of recurrence was 1 (4.2%) in contralateral lobe, 1 (4.2%) in central lymph node, 20 (83.3%) in central lymph node, and 2 (8.7%) in distant metastasis, managed by completion thyroidectomy, neck dissection, and radioactive iodine ablation, which was similar to our study. In contrast, Huang H. [18] reported a recurrence rate of 11.38% (14) of which one patient died due to pulmonary metastasis, six cases recurrence in the opposite lobe, six cases locoregional cervical lymph node metastasis, and one patient with superior mediastinal, level seven cervical lymph node metastasis, all recurrent cases managed by completion thyroidectomy, neck dissection, and radioactive iodine ablation, and 10 years' recurrence-free survival rate of 83.2% parallel to our paper. Perros P [1] reported a locoregional recurrence rate after H.T. of approximately 6%, and management included completion thyroidectomy, neck dissection, and RAI; our study showed a recurrence rate of 5.835%. Bosset M. [8] reported the type of recurrence according to tumor size: ≤4 cm (261 patients) and >4 cm (34 patients), in accordance with the 8th ATA guideline for thyroid tumor classification. Their recurrence was 40 (13.6%), which was divided into tumor size, locoregional 23 (57.5%), of which 19 (82.6%) were in tumor size ≤4 cm, and 4 (17.4%) were in tumor size >4 cm, metastasis 3 (7.5%), 0 in tumor size≤4 cm and 3 (100%) in tumor size >4 cm, contralateral micro-PTC 14 (7.5%), 12 (85.7%) in tumor size ≤4 cm and 2 (14.3%) in tumor size >4 cm. All recurrence cases were managed in accordance with the ATA 2015 guidelines, which were similar to those in our paper. Geron Y.'s [8] research paper displayed that recurrence of the hemithyroidectomy group was 6 (6.1%), and all-cause mortality was 6 (6.1%); in the total thyroidectomy group, recurrence was 1(2.3%), and all-cause mortality was 7 (14%),

dissimilar to our study but management of recurrent cases following ATA guideline similar to our work. Matsuzu K [26] reported that T.T. is the first to undergo earlier neck irradiation. The family history of PTC, capsular invasion, neck node metastasis, and recurrence cases were managed with neck dissection and RAI, as in the present study.

5. CONCLUSION:

T.T. has several advantages of SLPTC; for the most significant patient, who has one operation and RAI with age≥45-≥55 years, family history, and capsular invasion, with lifelong follow-up and suppressive dose of levothyroxine. On the other hand, H.T. is effective in the low-risk group of SLPTC; aside from follow-up, they need no treatment, and preservation of the gland leads to normal health and reproductive life. In this study, the mean age and SD of the H.T. group were 31.50±8.074 years. However, the recurrence rate is slightly higher in H.T. than in T.T. Statistical data showed both H.T. and T.T. are significant, but highly significant in T.T.

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CONFLICT OF INTEREST:

The authors declare no conflict of interest.

STATEMENT OF INFORMED CONSENT:

Informed consent was taken from the patient and their parents or close relatives.

Ethical Approval: Approved.

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