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Effect and long-term outcome of hemithyroidectomy for patients with low-risk papillary thyroid carcinoma

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Abstract

Background

Although the incidence of papillary thyroid carcinoma (PTC) has increased during the recent years, most of the PTCs are slow growing and considered as low-risk tumors with an excellent prognosis. This observed increase in small tumors leads to many controversies regarding the optimal surgical approach, and the extent of surgery for low-risk PTC is still the subject of debate. Recently, there is a trend toward utilizing a less-aggressive surgical approach, including the option of hemithyroidectomy for small PTCs up to 4 cm.

Patients and methods

This study included 60 patients with a proven diagnosis of PTC. According to the guidelines of the British Thyroid Association, the American Thyroid Association, and the American Joint Committee on Cancer, these patients would have low-risk PTCs and considered eligible for hemithyroidectomy (total lobectomy with isthmusectomy) as an initial treatment and followed up for about 5 years to detect recurrence and survival rate.

Results

Hemithyroidectomy was performed as an initial treatment. Completion thyroidectomy (CTx) was performed in five (8.33%) patients in the postoperative period within 1 week after the initial operation owing to identifying high-risk features in the final histopathology. During the follow-up period of the 60 patients, there was no locoregional recurrence. Recurrence was observed in three (5%) patients in the contralateral thyroid lobe within 3–4 years and was treated with a second surgery in the form of CTx. The overall rate of CTx was eight (13.33%) of 60 patients. The prognosis and the 5-year survival rate were excellent (100%).

Conclusion

Hemithyroidectomy in appropriately selected patients is an optimal surgical approach for treating low-risk PTC, and if recurrence occurs in the contralateral lobe, it can be treated safely by CTx, which yielded excellent curative results.

Keywords: Completion thyroidectomy, hemithyroidectomy, low-risk papillary thyroid carcinoma, recurrence

INTRODUCTION

Thyroid cancer is considered the most prevalent endocrine malignancy worldwide, with steadily increasing incidence in the USA and several countries [1]. In Egypt, the estimated number of incidence and prevalence of thyroid cancer is very similar to Western countries [2].

Papillary thyroid carcinoma (PTC) is a differentiated thyroid cancer derived from follicular epithelium, accounting for ~80–90% of all thyroid cancers [3].

The wide availability can explain this current increase in incidence and use of diagnostic techniques like high-resolution

neck ultrasonography, fine-needle aspiration (FNA) cytology, and computed tomography [4].

Despite this increase in incidence, the long-term prognosis is usually excellent, with 5–10-year survival rates up to 98% [5,6].

Surgery is the cornerstone of treatment for patients with PTCs, and total thyroidectomy is the treatment of choice for tumors more than 4 cm or less than 4 cm with high-risk features.

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However, the classical regimen of treating all patients with PTC with total thyroidectomy, prophylactic neck dissection, and radioactive iodine (RAI) became no longer suitable for PTC 1–4 cm with low-risk features [7,8].

Until now, there is no universal consensus about the extent of surgery, and there is still a discussion about the optimal treatment for unilateral low-risk PTCs with much controversy on the long-term outcome and recurrence rates following hemithyroidectomy [9,10].

Because the extent of surgery for PTC is still a topic of active debate, we aimed in this prospective study to evaluate the outcome of hemithyroidectomy as an initial surgical approach for the treatment of patients with low-risk PTC 1–4 cm concerning recurrence and overall survival.

PATIENTS AND METHODS

Patient selection

The study was approved by the institutional Ethics Committee of El-Sahel Teaching Hospital. This prospective cohort study is conducted at the Al-Ahrar and El-Sahel Teaching Hospitals between April 2014 and July 2016 and included 60 patients with a proven diagnosis of low-risk PTC. Their age ranged from 24 to 55 years (the mean age was 35 ± 8 years). Patient selection was performed following the inclusion and exclusion criteria of the British Thyroid Association (BTA), American Thyroid Association (ATA) and the American Joint Committee on Cancer (AJCC) guidelines.

The inclusion criteria included age up to 55 years, tumors confined to one lobe, size ranged from 1 to 4 cm, absence of extrathyroidal extension (ETE), and lymph node metastasis. To minimize the risk of recurrence, we excluded patients with any of the following known high-risk features: age more than 55 years, tumors more than 4 cm, bilateral nodularity, evident lymph node metastases, and history of neck irradiation or positive family history.

We also excluded patients who were lost during the period of follow-up.

A preoperative discussion with all the patients was done, and informed consent was taken regarding the possibility of secondary operative intervention in the postoperative first week or during the follow-up period.

Surgical approach

Study participants underwent hemithyroidectomy (total lobectomy with isthmusectomy) through the following main principles: a direct thyroidectomy 4–5-cm incision was done to minimize postoperative pain and avoid unnecessary neck exploration. For more exposure, the fascia over the sternomastoid muscle's anterior surface is dissected to allow comfortable lateral traction of infrahyoid muscles. The tracheal surface above and below the isthmus is dissected; the isthmus is then divided to facilitate the mobility of the thyroid lobe. The paratracheal space is entered with early identification and

safeguarding the recurrent laryngeal nerve and parathyroid glands. The thyroid lobe is excised using the extracapsular technique.

Indications for completion thyroidectomy

Operative specimens were examined microscopically and assessed for the following histopathological features: cell type, ETE, tumor size, and vascular invasion. If the final histopathology reports identify any High Risk Factors (HRFs) such as positive tumor margins, index tumor more than 4 cm, and aggressive histopathology, this would be considered an indication for completion thyroidectomy (CTx) to improve the clinical outcome.

Postoperative follow-up and outcome

After hospital discharge, all patients underwent regular follow-up visits every month in the first 3 months, and then at a 6-month interval up to nearly about 5 years (mean follow-up was 55 months) aiming to evaluate the response to the surgical approach concerning recurrence and survival rate. The follow-up included regular clinical evaluation with physical neck examination and serial neck ultrasonography to detect any locoregional recurrence or future nodules in the contralateral thyroid lobe and evaluate regional lymph nodes. Thyroid hormone assay, including thyroid-stimulating hormone (TSH), was done initially every month. Every 3–6 months after surgery, L-thyroxine was individually administered in a suppressive dose of TSH that prevents thyroid nodular hyperplasia and avoids the risk of subclinical thyrotoxicosis.

Statistical analysis

Data were summarized and presented as mean \pm SD for quantitative variables, and number and percentage for categorical variables.

RESULTS

The baseline features and tumor characteristics of the 60 patients enrolled in this study with the BTA-defined, ATA-defined, and AJCC-defined low-risk PTCs are shown in Table 1. There were 22 (36.67%) males and 38 (63.33%) females.

Patients' age at the time of presentation ranged from 24 to 55 years, and the mean age was 35 ± 8 years. Tumor size ranged from 1 to 4 cm, with a mean size of 2.3 ± 0.9 cm.

Final postoperative histopathological findings were as follows: of the 60 patients who underwent hemithyroidectomy, five patients were found to have high-risk features in the final postoperative histopathological examination (Table 2).

Early completion thyroidectomy

Of the 60 patients eligible for initial hemithyroidectomy, five (8.33%) patients underwent CTx within 1 week in the postoperative period owing to identifying one or more high-risk features in the final histopathological specimens. The operation was performed easily because the contralateral lobe to be excised was intact and did not touch in the initial operation

with no disturbed anatomy.

Late completion thyroidectomy (recurrence)

In our study, there was no locoregional recurrence in the thyroid bed of the resected thyroid lobes in the 60 patients during the follow-up period, either in the 55 patients with hemithyroidectomy or five patients with CTx. However, three (5%) patients developed recurrence in the contralateral lobes within 3–4 years after the initial surgery. In these patients, CTx was performed safely with a complete cure with no evidence of recurrence (Table 3).

In 52 (86.67%) patients, hemithyroidectomy was enough for the complete cure of the tumor. CTx was needed in eight (13.33%) patients owing to unfavorable postoperative final pathology or late recurrence in the contralateral lobes.

Regarding L-thyroxine replacement and TSH suppressive therapy, L-thyroxine was needed in only 12 (20%) patients. Among 55 patients with an excellent response to initial hemithyroidectomy, five patients did not show sufficient thyroid hormone release from the contralateral lobe and had the TSH in the low-average level, so L-thyroxine was given in a dose to maintain TSH level between 0.5 and 2 µl. In seven patients who underwent CTx because of the final histopathological diagnosis of high-risk features or due to recurrence, L-thyroxine was given in a dose to maintain TSH suppression level in the range 0.1–0.5 µl.

Postoperative complications

In the 60 patients with initial hemithyroidectomy, transient Recurrent Laryngeal Nerve (RLN) injury was observed in one (1.66%) patient. One (12.50%) patient of eight patients who underwent CTx had transient RLN injury after CTx. There was no permanent RLN injury during the period of study.

The rate of transient hypoparathyroidism after the initial hemithyroidectomy was zero. Among the eight patients who underwent CTx, one (12.50%) patient had minimal symptoms of transient hypoparathyroidism, and the rate of permanent hypoparathyroidism was zero (Table 4).

DISCUSSION

Thyroid cancer is considered to be the most prevalent endocrine malignancy worldwide, with steady increase in the incidence in the USA and several countries [1].

According to the Egyptian National Cancer Institute report, primary thyroid malignancy is the most prevalent endocrine tumor in Egypt, and PTC is the most common type, accounting for 70.94% of all thyroid cancers [2].

This increased PTC incidence is mainly attributed to the widespread use of diagnostic tools like neck ultrasound and ultrasound-guided FNA [4].

The PTC is a well-differentiated tumor with an excellent survival rate. In the management of PTC, the main goal is to avoid the risk of disease recurrence. When evaluating the risk

Table 1: The patients’ baseline features and tumor characteristics

Features	n (%)
Sex	
Male	22 (36.67)
Female	38 (63.33)
Age (years)	
24-45	54 (90.0)
46-55	6 (10.0)
Tumor size	
1-2 cm	4 (6.67)
2-3 cm	16 (26.67)
3-4 cm	40 (66.67)
Extrathyroidal extension	0
Lymph node metastases	0

Table 2: The final histopathology of the hemithyroidectomy patients with identified high-risk factors of patients who would have required completion thyroidectomy

Postoperative final histopathology	n (%)
Low-risk histopathology	55 (91.67)
High-risk histopathology	
Positive tumor margins	2 (3.33)
Aggressive histopathology	2 (3.33)
Index tumor >4 cm	1 (1.67)
Total	60 (100)

Table 3: The final results of the response to hemithyroidectomy as an initial surgical approach for treating low-risk papillary thyroid carcinomas

Operation type	n (%)
Hemithyroidectomy (best response)	52 (86.67)
Completion thyroidectomy	
Early completion thyroidectomy	5 (8.33)
Late completion thyroidectomy	3 (5.0)
Total	60 (100)

Table 4: Postoperative complications

Complication	Initial hemithyroidectomy [n (%)]	CTx [n (%)]
RLN injury		
Transient	1 (1.66)	1 (12.50)
Permanent	0	0
Hypothyroidism		
Transient	0	1 (12.50)
Permanent	0	0

CTx, completion thyroidectomy.

of recurrence, PTC is classified into three main pathological classes: low risk, intermediate, and high-risk class according to age, family history, multifocality, ETE, histopathological features, and lymph node metastasis [11].

The standard management of PTC is surgical excision. In

2009, the ATA guidelines and much previous research had recommended total thyroidectomy as the primary surgical treatment for all PTCs even without the evidence of high-risk features, ETE, or distance metastases [12]. However, several retrospective studies had found equivalent survival outcomes in patients with tumors measuring 1–4 cm without high-risk features who underwent hemithyroidectomy or total thyroidectomy [5,13,14].

As a result, the BTA in 2014 and recent clinical guidelines of the ATA in 2015 proposed hemithyroidectomy as a less extensive operative approach for patients with low-risk PTCs measuring 1–4 cm [8,15].

In practice, the BTA and ATA recommendation guidelines' response was unclear with conflicting data still exciting yet about the extent of surgery, ensuring oncologic completeness for PTC of 1–4 cm. The surgical approaches may consist of either total thyroidectomy or total lobectomy with isthmusectomy [16–18].

Several studies have routinely recommended total thyroidectomy sometimes associated with neck dissection and/or postoperative RAI therapy for treatment of 1–4 cm low-risk intrathyroidal PTCs owing to its advantages in improving survival, lower risk of recurrence, and decreased follow-up burden [19–21]. However, this traditional strategy for patients with low-risk PTC has not been accepted [22].

The recent guidelines do not recommend routine central neck lymph node dissection without lymph node metastasis evidence on clinical neck examination, preoperative imaging studies, and FNA-guided ultrasonography.

Furthermore, RAI ablation therapy has no effect on recurrence or survival in low-risk PTC, and prophylactic lymph node dissection may be associated with a higher incidence of recurrent laryngeal nerve injury and permanent hypoparathyroidism [23,24].

These data lead to a shift toward an alternative, less-aggressive approach, hemithyroidectomy, for low-risk tumors [25,26].

The study of Kim *et al.* in 2017 [27] has the opinion that these patients are being over-treated and exposed to higher risks of complications.

A more recent study by Vargas-Pinto and Romero Arenas [28] confirmed that there is no definite advantage regarding the improvement in both recurrence and survival rates in low-risk patients treated with more aggressive approaches other than hemithyroidectomy; this study demonstrates that hemithyroidectomy alone is the adequate initial treatment for low-risk PTC with the advantage of fewer complications without increased risk of cancer recurrence.

The low-risk PTCs include tumors 1–4 cm confined to one lobe without ETE or cervical lymph node metastases in patients aged less than 45 years without a family history or history of neck irradiation. However, the AJCC has increased the age for

the diagnosis of low-risk PTC from 45 to 55 years, and this leads to the downstaging of 12% of patients into a low-risk class without significantly altering the recurrence and survival rate [29,30].

In our study, we evaluated the effect and long-term outcome of patients with low-risk PTC selected according to the BTA and ATA guidelines and are treated with hemithyroidectomy as an initial line of treatment. According to the AJCC, six (10%) patients of their age ranged from 46 to 55 years were classified as low-risk PTC and included in the study.

For low-risk PTC treatment, hemithyroidectomy has several advantages over total thyroidectomy, including shorter operative time, less risk of bilateral RLN injury and permanent hypoparathyroidism, and a better quality of life. Moreover, fewer patients may need thyroid hormone replacement therapy [31].

Polistena *et al.* [32] found that more extensive surgery (i.e., total thyroidectomy vs. hemithyroidectomy, lymph nodes dissected vs. not dissected) is correlated with increased rates of bilateral RLN injury and permanent hypoparathyroidism. The reported incidence of vocal fold paralysis in patients with total thyroidectomy for well-differentiated thyroid cancer may be up to 9.5%, and also, the incidence of permanent hypocalcemia was high as 5.4% in patients who have had total thyroidectomy with or without central lymph node resection for well-differentiated thyroid cancer [33,34].

Our present study confirms that the rate of these two postoperative complications was very low. In our series of 60 patients with PTC managed by initial hemithyroidectomy, transient RLN was observed in one (1.66%) patient; the symptoms were minimal and disappeared within 1 month with no need for intubation. One (12.50%) patient of eight patients who underwent CTx had transient RLN injury after CTx, and there was no permanent RLN injury.

The rate of transient hypoparathyroidism in the initial hemithyroidectomy (60 patients) was zero. Among eight patients who underwent CTx, one (12.50%) patient had minimal symptoms of transient hypoparathyroidism in the form of circumoral numbness and received oral calcium for 2 weeks with a complete cure. The rate of permanent hypoparathyroidism was zero.

Total thyroidectomy patients always require lifelong thyroid hormone replacement therapy [35]. In our study, only 12 (20%) patients (four from 55 patients with excellent response to initial hemithyroidectomy plus eight patients with CTx patients) required L-thyroxine hormone therapy to reach the TSH level required to prevent thyroid hyperplasia and avoid the risk of subclinical thyrotoxicosis.

Despite the advance in preoperative neck ultrasonography, FNA biopsy, and intraoperative frozen section examination of the thyroid nodules, the final classification of PTC's risk stratification and the decision-making process of CTx

can be only accurately determined after reviewing the final histopathological features of the resected lobe [36,37].

According to the ATA guidelines and the AJCC staging system for managing low-risk PTC, about 11% of patients undergoing hemithyroidectomy as an initial operation would require CTx because of aggressive histopathology [38].

In our study, five (8.33%) of 60 patients underwent CTx after 1 week of the initial operation because of the resected lobe's final aggressive histopathological features.

Several research studies have investigated the risk of recurrence after hemithyroidectomy. Vaisman *et al.* [39] evaluated 72 patients who underwent hemithyroidectomy and found the recurrent disease in only three (4.2%) patients, all of whom achieved no evidence of cancer after CTx. Li *et al.* [40] reported an incidence of 4.6% recurrence in 129 patients after hemithyroidectomy. The study of Kim *et al.* [41] included 147 patients with 1–4-cm PTCs who underwent hemithyroidectomy compared with 298 patients who underwent total thyroidectomy with a median follow-up period of 7 years. There was no significant difference in recurrence rates. The recurrence was reported in nine (6.1%) patients for PTC tumors 1–4 cm treated with hemithyroidectomy versus 17 (5.7%) patients treated with total thyroidectomy.

Huang *et al.* [42] observed 123 patients with unilateral multifocal PTC after hemithyroidectomy. The recurrence was found in the contralateral thyroid lobe of six (4.88%) patients. The mean time of recurrence was 96 months and required a secondary surgery resecting the contralateral lobe.

There was no locoregional recurrence in the thyroid bed of the resected thyroid lobes in the 60 patients during follow-up in our study. This may be attributed to the proper selection of the patients with low-risk PTC following the BTA and ATA selection criteria and the extracapsular technique's meticulous use.

However, in the 55 hemithyroidectomy patients, three (5.4%) patients developed recurrence in the contralateral lobes within 3–4 years after the initial operation. In our study, the recurrence rate is nearly similar to the studies mentioned above; the disease picked up during follow-up by high-resolution imaging ultrasound reveals thyroid nodules in the remnant contralateral lobe. CTx treats these patients with complete cure with no evidence of recurrence or effect on survival.

The recent studies by Mainthia and Lubitz [43] and Ullmann *et al.* [44] demonstrated that total thyroidectomy as a treatment option for low-risk PTCs measuring 1–4 cm does not prove a significant benefit in disease-specific survival compared with hemithyroidectomy.

More recent evidence by Suman *et al.* [45] approved that hemithyroidectomy can be performed in patients with low-risk PTC with excellent disease-specific survival rates, and if a second operation is required because final postoperative histopathology reveals high-risk features or due to recurrence, CTx is an available safe option without the effect on survival.

Our study's finding is consistent with other studies' results, as mentioned before, which suggested that a more conservative approach for patients with low-risk PTCs may be a more appropriate management strategy, despite the slight risk of the need for CTx.

CONCLUSION

The present study results favor the latest ATA and BTA guidelines suggesting to perform a less-aggressive treatment for most low-risk PTCs. This study approved that hemithyroidectomy for low-risk PTCs carries excellent survival. When a secondary operative procedure is required because of aggressive final histopathological features or recurrence in the contralateral lobe, CTx can be performed safely. Our study supports hemithyroidectomy as the preferred surgical approach for low-risk PTCs. However, careful patient selection is essential to achieve the best results.

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Conflicts of interest

There are no conflicts of interest.

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