Original Article

Intraoperative frozen section for determining the extent of surgery in papillary thyroid carcinoma: comprehensive risk factor assessment

Chaoyu Jiang[1#], Yongzhao Chen[2#], Chen Zhang[1#], Bo Jiang[1], Cheng Qu[1], Guanqun Dong[3], Yanxue Wang[4], Ru Wang[1], Yuqian Luo[5], Jianfeng Sang[1], Lei Su[1]

[1]Division of Thyroid Surgery, Department of General Surgery, Nanjing Drum Tower Hospital, the Affiliated Hospital of Medical School, Nanjing University, Nanjing, China; [2]Nanjing Drum Tower Hospital Clinical College of Nanjing University of Chinese Medicine, Nanjing, China; [3]Medical School of Southeast University Nanjing Drum Tower Hospital, Nanjing, China; [4]Nanjing Drum Tower Hospital, Affiliated Hospital of Medical School, Nanjing University, Nanjing, China; [5]Department of Pathology and Laboratory Medicine, Nanjing Drum Tower Hospital and Jiangsu Key Laboratory for Molecular Medicine, Nanjing, China

Contributions: (I) Conception and design: C Jiang, Y Luo, L Su; (II) Administrative support: J Sang, L Su; (III) Provision of study materials or patients: B Jiang, J Sang, L Su; (IV) Collection and assembly of data: C Jiang, G Dong, C Qu; (V) Data analysis and interpretation: Y Chen, C Zhang, Y Wang; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Yuqian Luo, MD. Department of Pathology and Laboratory Medicine, Nanjing Drum Tower Hospital and Jiangsu Key Laboratory for Molecular Medicine, 321 Zhongshan Road, Nanjing 210008, China. Email: yuqianluo31@foxmail.com; Jianfeng Sang, MD; Lei Su, MD. Division of Thyroid Surgery, Department of General Surgery, Nanjing Drum Tower Hospital, the Affiliated Hospital of Medical School, Nanjing University, 321 Zhongshan Road, Nanjing 210008, China. Email: drsangjianfeng@163.com; suleinjglyy@sina.com.

Background: There is much debate on the optimal treatment approach of papillary thyroid carcinoma (PTC). Different guidelines base recommendations on various risk factors. While diagnosing the various risk factors is difficult due to the technical limitations, intraoperative frozen section (IFS) may be a feasible method. We aim to real-time evaluate the multiple risk factors, including lymph node metastasis (LNM), extrathyroidal extension (ETE), multifocality using IFS, and then identify a more effective surgical plan, which may help avoid the need for a second surgery and improve prognosis of patients.

Methods: We retrospectively reviewed the medical records of 364 patients from January 1, 2021 to December 31, 2021. All the patients were initially recommended to undergo a hemithyroidectomy (HT) with isthmusectomy and ipsilateral central compartment neck dissection (CCND). IFS would be executed immediately. Further total thyroidectomies (TTs) would be performed if: (I) results of IFS showed >5 LNM, or (II) there are 1≤ LNM ≤5 but with ETE and/or multifocal carcinoma. The patients were divided and investigated according to the extent of surgery.

Results: Based on the results of IFS, 72 patients underwent TT. The TT group displayed larger average tumor diameter, greater age, higher average body mass index (BMI), and elevated incidence of hypertension and hyperlipidemia compared to the HT group. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of IFS were 77.61%, 100%, 100%, and 88.46%, respectively.

Conclusions: IFS is a highly reliable procedure. Comprehensively evaluating central compartment LNM, ETE, and multifocal carcinoma through IFS helps identify a more reasonable surgical option under the current clinical consensus, which may thus help avoid the need for a second surgery.

Keywords: Papillary thyroid cancer (PTC); intraoperative frozen section (IFS); multiple risk factors; lymph node metastases (LNMs)

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Introduction

Thyroid cancer, particularly papillary thyroid carcinoma (PTC), has been on the rise globally (1). Despite PTC's biologically indolent behavior and favorable prognosis, there is a lot of debate on the optimal treatment approach (2,3). Different guidelines base their recommendations on various risk factors (4,5). Conservative treatment with unilateral thyroidectomy is favored in low-risk cases to reduce surgical trauma and postoperative complications (6). However, PTC tends to metastasize to lymph nodes (LNs), with central compartment LNs being the most common site of metastasis (7). Neck lymph node metastasis (LNM), especially the lateral LNM, is the primary risk factor for PTC metastasis and recurrence (8). Preoperative assessment of neck LN status is typically performed with ultrasound. However, diagnosis of central compartment LNs involvement is difficult due to the unique anatomy and technical limitations of color Doppler ultrasound (9). Studies have reported that the detection rate of central compartment LNs by color Doppler ultrasound is only 20% to 31% (9-11). Intraoperative frozen section (IFS) has been reported to provide a relatively accurate evaluation of the situation of the central compartment LNs (12-14).

Radioactive iodine (RAI) and surgical scope

Some guidelines suggest RAI for patients with >5 LNM, as they are considered to have a higher risk of recurrence and metastasis, requiring total thyroidectomy (TT) (4,5). However, we have found that many patients have ≤5 LNM in practical work. Are they not in danger? As we know extrathyroidal extension (ETE) and multifocal carcinoma are also significantly associated with poor PTC prognosis (15,16). So, the number of LNM and cancerous lesions, ETE are critical factors for intraoperative decision-making and determining the surgical scope. IFS may be a feasible method (17). However, few studies comprehensively consider multiple risk factors and determine the surgical scope through IFS evaluation.

Study objectives

This study aims to comprehensively consider various risk factors and evaluate them through IFS to select a more reasonable surgical plan, thereby avoiding possible secondary surgery. Our focus was on evaluating multiple risk factors, including central compartment LNM, ETE, multifocality, through IFS. We analyzed the impact of these factors on surgical decisions and the surgical scope. Our goal was to identify a more effective surgical plan that may help avoid the need for a second surgery, thus reduce the risk of recurrence and metastasis in PTC patients. We present this article in accordance with the STROBE reporting checklist (available at https://gs.amegroups.com/article/view/10.21037/gs-23-182/rc).

Highlight box

Key findings
- Comprehensively considering various risk factors and evaluating them through intraoperative frozen section (IFS) help select a more reasonable surgical plan.

What is known and what is new?
- There is a debate on the optimal extent of surgery in papillary thyroid carcinoma (PTC).
- Comprehensively considering various risk factors and evaluating by IFS helps surgical determination.

What is the implication, and what should change now?
- Comprehensively considering various risk factors and evaluating them through IFS help determine the extent of surgery in PTC, thereby avoiding possible secondary surgery.

Methods

Target patients

We retrospectively reviewed the medical records of 2,039 patients who had surgery to remove their thyroid at Nanjing Drum Tower Hospital during the period of January 1, 2021 to December 31, 2021. To be included in the study, patients had to have had certain preoperative examinations and be diagnosed with a specific type of thyroid cancer. We excluded patients who had previously undergone thyroid surgery or had a history of neck trauma, as well as those outside of the age range of 18 to 80 years. Ultimately, our study included 364 patients who underwent a specific type of thyroid surgery and had their thyroid tissue and LNs examined during the surgery. We analyzed the patients' medical data, including their age, gender, imaging tests, blood test results, cancer stage, and body mass index (BMI), among other factors.

Approach to pathology

The excised thyroid lobes, isthmuses, and central compartment LNs were subjected to IFS and postoperative routine pathology (PR). The IFS examination was carried out expeditiously within 30 minutes, and the outcomes were promptly reported. The report encompassed tumor histotype, ETE, multifocality, as well as the number of LNM and the number of LNs retrieved. PR results were issued within 14 days. The IFS and the PR were both performed by seasoned pathologists, each having more than 15 years of clinical pathology experience.

Preoperative work-up

Before surgery, all patients were subjected to a comprehensive preoperative examination, including physical examination, thyroid ultrasound, supraclavicular LNs ultrasound, serum biochemistry, ultrasound-guided fine-needle aspiration biopsy, and genetic testing. The preoperative thyroid ultrasound was conducted by highly specialized ultrasound physicians who have more than 20 years of experience in thyroid ultrasound, using a state-of-the-art Resona 7Elite ultrasound apparatus (Mindray, Shenzhen, China). In all patients, the thyroid ultrasound revealed nodules of thyroid imaging reporting and data system (TI-RADS) level 4 or higher in a single thyroid lobe, while nodules of TI-RADS level 1–3 with a diameter less than 1.5 cm or TI-RADS level 4 or higher nodules were absent in the contralateral thyroid lobe.

Surgery

Physicians with over 20 years of experience in thyroid surgery performed the procedure. All patients were initially recommended to undergo a hemithyroidectomy (HT) with isthmusectomy and ipsilateral central compartment neck dissection (CCND). The central compartment LNs are defined as the neck level 6 LNs (pretracheal, prelaryngeal, and paraesophageal LNs), including the LNs from the hyoid bone superior to the innominate (brachiocephalic) artery inferiorly. On each side, the lateral boundary was limited by the medial border of the carotid sheath. IFS were executed immediately. Following the surgical standards proposed by the center, further TTs would be performed if: (I) results of IFS showed >5 LNM, or (II) there are 1≤ LNM ≤5 but with ETE and/or multifocal carcinoma. Otherwise, the surgery concluded. Out of the total 364 patients, 292 underwent HT with isthmusectomy and ipsilateral CCND, while 72 patients required further contralateral thyroid lobectomy.

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of the Nanjing Drum Tower Hospital, the Affiliated Hospital of Nanjing University Medical School (No. 2021-096-02), and individual consent for this retrospective analysis was waived.

Statistical analysis

All the data were analyzed using IBM SPSS Statistics version 20. Continuous data conforming to normal distribution were expressed by mean ± standard deviation (SD), while categorical data were reported as rates and proportions. Differences in categorical data were compared using χ^2 test or Fisher's exact test and the independent-sample *t*-test was performed for continuous data. Logistic regression analysis was used for multivariate analysis. A two-sided P value of <0.05 indicated a statistically significant difference.

Results

The present study reported on the baseline clinical characteristics and surgical outcomes of 364 patients with thyroid tumors (*Table 1*). Baseline characteristics, including age, gender, and maximum tumor diameter, were collected and analyzed. The mean age of the patients was 42.33±11.34 years, with a range of 22 to 70 years. The mean maximum tumor diameter was 0.87±0.53 cm, with a range of 0.1 to 3.0 cm.

The surgical procedure outcomes were shown in *Figure 1*. IFS was used to determine the extent of surgery required for each patient. One hundred and four patients had LNM. Four of them had >5 LNM and they had extended surgery as a result. One hundred patients had ≤5 LNM. Among them, 68 patients with ETE and(or) multifocality were performed TT according to our surgical strategy. Thirty-two patients had neither ETE nor multifocality, so they only need HT. Based on the results, 72 patients were performed TT, while the remaining 292 patients underwent HT.

Patients were evaluated according to the surgical extent as the HT group and TT group (*Table 2*). Comparative analysis revealed that the TT group had a larger average tumor diameter (1.25±0.62 *vs.* 0.78±0.46 cm, P<0.001), higher age (46.28±11.62 *vs.* 41.36±11.07 years, P=0.001), higher average BMI (24.95±3.81 *vs.* 23.46±3.60 kg/m^2, P=0.002), and a higher incidence of hypertension (24/48 *vs.* 29/263, P<0.001) and hyperlipidemia (28/44 *vs.* 58/234, P=0.001) compared to the HT group. Age, hypertension

Table 1 Clinicopathologic characteristics

Characteristics	Values
Number of patients	364
Sex, n (%)	
Male	111 (30.5)
Female	253 (69.5)
Age (years), mean ± SD [range]	42.33±11.34 [22–70]
Tumor size (cm), mean ± SD [range]	0.87±0.53 [0.1–3.0]
Total tumor size (cm), mean ± SD [range]	0.90±0.54 [0.1–3.3]
BMI (kg/m^2), mean ± SD [range]	23.75±3.69 [16.21–35.89]
Multiplicity, n (%)	38 (10.4)
Extrathyroidal extension, n (%)	202 (55.5)
Frozen analyses, mean ± SD [range]	
Number of retrieved LNs	3.51±3.45 [0–20]
Number of metastatic LNs	0.61±1.23 [0–8]
Permanent analyses, mean ± SD [range]	
Number of retrieved LNs	3.66±3.53 [0–20]
Number of metastatic LNs	0.74±1.29 [0–8]
TNM classification, n (%)	
T stage	
T1a/1b/2/3a/3b	266/78/13/0/7 (73.1/21.4/3.6/0/1.9)
N stage	
N0/1/1a/1b/x	195/14/116/4/35 (53.6/3.8/31.9/1.1/9.6)
M stage	
M0	364 (100.0)
Stage I/II, n (%)	344/20 (94.5/5.5)

SD, standard deviation; BMI, body mass index; LNs, lymph nodes; TNM classification, tumor node and metastasis classification.

and hyperlipidemia were included in multivariate analysis with ETE and multifocality; as shown in *Table 3*, ETE [P<0.001; odds ratio (OR) =22.550] and multifocality (P=0.048; OR =2.416) are independent risk factors between HT and TT groups after adjusting for age, hypertension and hyperlipidemia.

The diagnostic accuracy of IFS for central compartment LNs was evaluated in 364 patients (*Table 4*). The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the frozen analyses were 77.61% (104/134), 100% (230/230), 100% (104/104), and 88.46% (230/260), respectively.

Among the 364 patients, 52 (14.29%) had a discrepancy in the number of LNs retrieved between IFS and PR, with 36 patients of them had more LNs retrieved during PR. Furthermore, there were 36 cases in which the number of LNM detected in IFS differed from that found in PR, and all of them had more LNM during PR (*Figure 2*).

Pathological analysis of the contralateral lobe was performed on the 72 patients who underwent TT (*Table 5*). Among them, 24 cases were found to have cancer in the contralateral lobe, with only one case (1/24) had >5 LNM, as determined by both IFS and PR. Thirty-four cases were found to have benign lesions, only one case (1/34) had >5 LNM, as determined by both IFS and PR.

Discussion

The selection criteria for surgical scope in PTC are constantly evolving as research deepens. However, the fundamental idea is to consider the risk factors associated with PTC prognosis. Despite this, there is still relatively little research that comprehensively considers various risk factors. IFS, which has high accuracy and data support, is currently a more mature technology (18,19). By prompting various risk factors through IFS during surgery, more accurate surgical plans can be formulated during the initial surgery, which can improve patient prognosis.

In this study, all patients underwent IFS. According to the pathological results, 72 patients underwent TT, and this group of patients was classified as the TT group, while the remaining 292 patients were classified as the HT group. We collected relevant clinical data from the patients and performed statistical analysis, and significant differences were observed between the TT and HT groups. Firstly, the tumor diameter in the TT group was larger. Tumor size is important for staging different tumors. A larger PTC tumor always corresponds to a poorer prognosis and an increased amount of neck LNM (20). At the same time, high BMI and high body fat rate are two major related factors of PTC (21), with overweight individuals having a 1.7 times increased risk of developing PTC and obese individuals having a 4.2 times increased risk compared to those of normal weight (22). In this study, the TT group had a higher BMI and a higher incidence of combined hyperlipidemia. Furthermore, the TT group had older age, which is consistent with the results of existing studies on risk factors for thyroid cancer

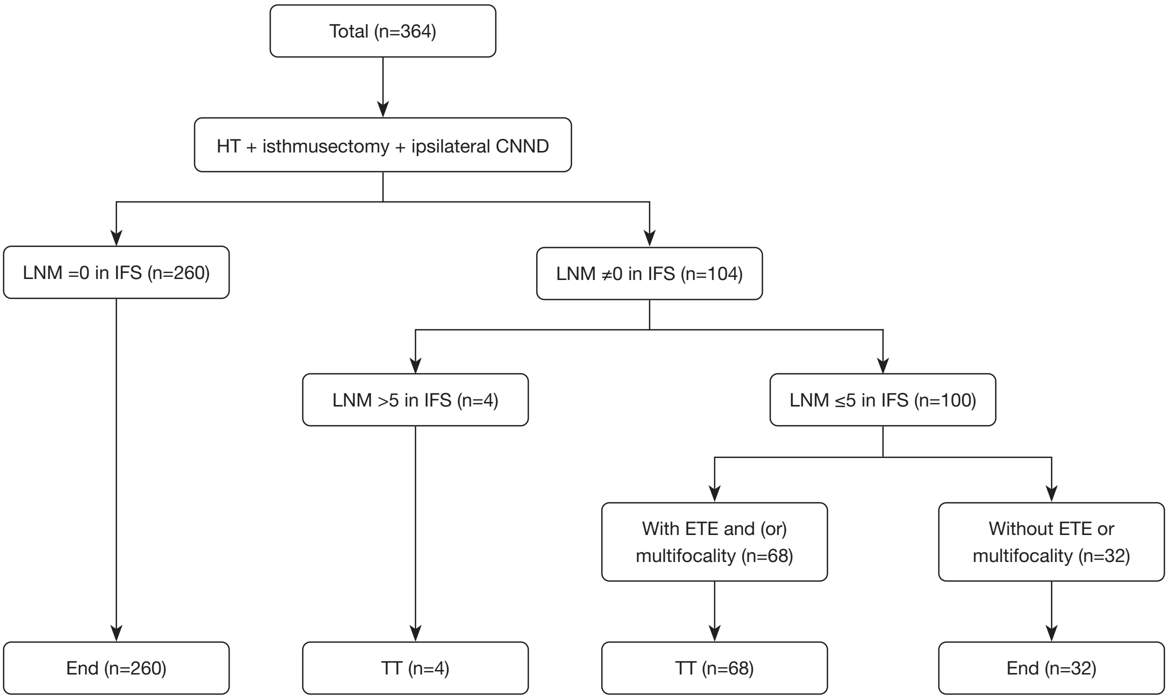

Figure 1 The surgical procedure outcomes. HT, hemithyroidectomy; CCND, central compartment neck dissection; LNM, lymph node metastasis; IFS, intraoperative frozen section; ETE, extrathyroidal extension; TT, total thyroidectomy.

Table 2 Analysis of patients according to the type of surgical procedure.

Characteristics	HT	TT	P value
Number	292	72	
Sex, n			0.765
Male	88	23	
Female	204	49	
Age (years), mean ± SD [range]	41.36±11.07 [22–70]	46.28±11.62 [22–66]	0.001
Tumor size (cm), mean ± SD [range]	0.78±0.46 [0.10–3.00]	1.25±0.62 [0.30–2.80]	<0.001
Total tumor size (cm), mean ± SD [range]	0.79±0.47 [0.10–3.30]	1.32±0.61 [0.40–2.80]	<0.001
BMI (kg/m^2), mean ± SD [range]	23.46±3.60 [16.21–35.89]	24.95±3.81 [17.56–34.64]	0.002
Hypertension, n (yes/no)	29/263	24/48	<0.001
Diabetes mellitus, n (yes/no)	16/276	6/66	0.531
Hyperlipidemia, n (yes/no)	58/234	28/44	0.001
Mutation in BRAF, n (yes/no)	283/9	64/8	0.010
Tumor location, n			0.310
Up	58	15	
Medium	170	47	
Down	64	10	

Table 2 (*continued*)

Table 2 (*continued*)

Characteristics	HT	TT	P value
Calcification in tumor, n (yes/no)	269/23	56/16	<0.001
Consistent of tumor, n			<0.001
Cystic	288	66	
Solid	3	0	
Mixed	1	6	
TSH (mIU/L), mean ± SD [range]	2.78±3.00 [0.01–42.3]	2.49±1.66 [0.19–12.1]	0.424
FT3 (pmol/L), mean ± SD [range]	4.65±0.60 [2.99–7.3]	4.82±0.65 [3.68–6.63]	0.043
FT4 (pmol/L), mean ± SD [range]	16.40±2.44 [6.90–26.5]	16.47±2.63 [12.4–23.3]	0.833
T3 (nmol/L), mean ± SD [range]	1.87±2.99 [1.01–52.3]	1.78±0.43 [1.30–4.65]	0.797
T4 (nmol/L), mean ± SD [range]	92.21±18.54 [1.60–203.00]	98.93±19.73 [61.00–177.00]	0.007
TG-Ab (IU/mL), mean ± SD [range]	98.23±290.79 [2.00–3,581.00]	106.02±326.05 [4.02–2,400.00]	0.843
TPO-Ab (IU/mL), mean ± SD [range]	48.82±109.44 [9.00–600.00]	28.35±77.86 [9.00–600.00]	0.070
TG (ng/mL), mean ± SD [range]	17.83±22.63 [0.20–300.00]	27.35±34.51 [0.20–226.00]	0.029
TNM classification, n			
T stage			<0.001
T1a/1b/2/3a/3b	233/50/5/0/4	33/28/8/0/3	
N stage			<0.001
N0/1/1a/1b/x	195/8/54/0/35	0/6/62/4/0	
M stage			–
M0	292	72	
Stage I/II, n	283/9	61/11	<0.001

HT, hemithyroidectomy; TT, total thyroidectomy; SD, standard deviation; BMI, body mass index; BRAF, BRAF V600E; TSH, thyrotropin; FT3, free triiodothyronine; FT4, free thyroxine; T3, triiodothyronine; T4, thyroxine; TG-Ab, thyroglobulin antibody; TPO-Ab, thyroid peroxidase antibody; TG, thyroglobulin; TNM classification, tumor node and metastasis classification.

Table 3 Multivariate analyses between HT group and TT group

Variables	Odds ratio	95% CI	P value
Age	1.002	0.972–1.032	0.911
Hypertension (yes/no)	3.905	1.851–8.238	<0.001
Hyperlipidemia (yes/no)	2.247	1.167–4.325	0.015
Multiplicity	2.416	1.009–5.785	0.048
Extrathyroidal extension	22.550	7.641–66.547	<0.001

HT, hemithyroidectomy; TT, total thyroidectomy; CI, confidence interval.

Table 4 Compare the results of lymph node metastases between IFS and PR

The results of lymph node metastases	PR^+	PR^-	PR total (PR^+ & PR^-)
IFS^+	104	0	104
IFS^-	30	230	260
IFS total (IFS^+ & IFS^-)	134	230	364

IFS, intraoperative frozen section; PR, postoperative routine pathology.

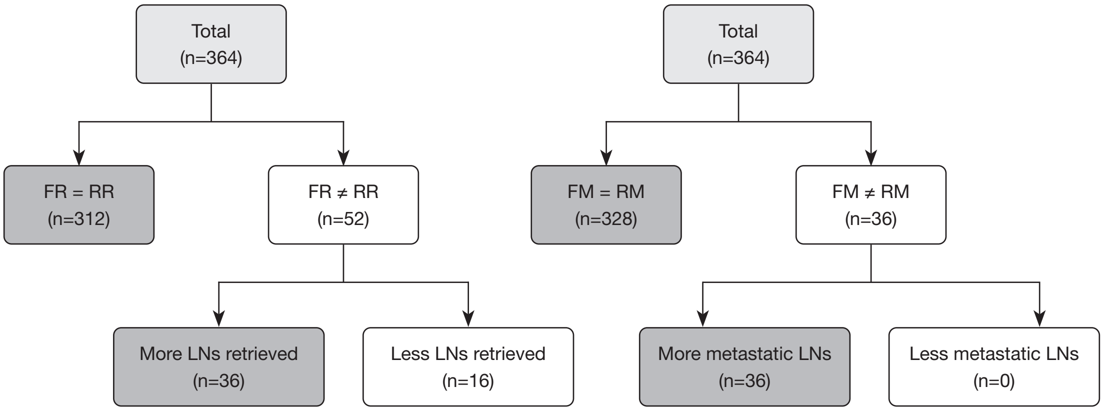

Figure 2 The results of intraoperative frozen section and postoperative routine pathology. FR, lymph nodes retrieved during intraoperative frozen section; RR, lymph nodes retrieved during postoperative routine pathology; FM, lymph node metastases during intraoperative frozen section; RM, lymph node metastases during postoperative routine pathology; LNs, lymph nodes.

Table 5 Analysis of pathology in the contralateral lobe

Description	FM ≤5	FM >5	Total
Normal tissue	12	2	14
Benign lesions	33	1	34
Cancer	23	1	24
Total	68	4	72

FM, lymph node metastases during intraoperative frozen section.

recurrence and metastasis. ETE and multifocality are independent risk factors between HT and TT groups after adjusting for age, hypertension and hyperlipidemia.

According to the National Comprehensive Cancer Network (NCCN) guidelines, patients with >5 LNM should consider TT (5). However, according to our surgical strategy, an additional 68 patients underwent TT. Of these 68 patients, 23 (33.82%) were found to have contralateral occult carcinoma, and these patients were able to avoid possible secondary surgery as a result. The other 45 (66.18%) patients did have a more extensive surgical procedure, while we can conduct further research to decrease proportion of them through additional screening. It is also necessary to further investigate whether patients who underwent TT have a more favorable prognosis.

Currently, guidelines determine the extent of surgery based on the main risk factors, such as the LNM in the neck, ETE, and multifocality (23-25). The LNM in the neck is one of the main factors determining the extent of surgery (26). Ultrasound remains the preferred method for assessing neck LNM, but ultrasound still has significant limitations in detecting and distinguishing metastatic LNs (27). There is also lower detection rate of involved LNs in the central compartment due to its unique anatomical location. Conventional methods for determining the presence of ETE and multifocality exhibit a relatively high incidence of missed diagnoses, particularly for small ETE and small lesions (28). It had shown that the sensitivity, specificity, PPV, and NPV of ultrasound in assessing ETE are lower than those of IFS (23).

We evaluated the results of the number of LNs retrieved between IFS and PR in the cohort of 364 patients. Among these 364 patients, 52 patients (14.29%) had inconsistent results and 36 patients of them had more LNs retrieved during PR. Following that, we assessed the results of the number of LNM. Thirty-six patients (9.89%) out of 364 had inconsistent results, and all of them had more LNM during PR. Interestingly, among these 36 patients (9.89%), 30 patients had opposite results between IFS and PR, which could affect the surgical approach. In fact, 21 patients failed to choose a larger range of surgical approach due to the opposite results between IFS and PR. These patients will be closely observed during follow-up. Similar to other study who reported the NPV of IFS as 96.1% (26), the NPV of IFS in our study was 88.46% (230/260). This suggests that IFS could be a reliable procedure even it has some limitations which may due to the skill of the operator.

Interestingly, this study found that among 72 patients who underwent total resection, 24 cases (33.33%) were found to have occult contralateral cancer during data collection, and only one of them had >5 LNMs (based on both IFS and PR). If the surgical scope were determined solely based on the number of LNM, the occult cancer in the other 23 patients would not have been detected. The existence of occult cancer cases highlights the limitation of ultrasound and the advantages of IFS. With the application of IFS, these 23 patients may avoid the possibility of a further operation. Hopefully, with more data to be collected in the future, we expect ourselves to reach more precise research result in the next stage.

IFS has a certain missed diagnosis rate, as it relies on a short inspection time and limited sample collection. However, we believe that the current missed diagnosis rate is still acceptable. Nevertheless, this study has some limitations. Firstly, it was a single-center retrospective study, and a multicenter study with a larger sample size may improve accuracy. Secondly, the sample size in this study was relatively small, and further sample expansion is needed to confirm the results. Finally, no follow-up had been conducted in this study, and subsequent follow-up of the enrolled patients is needed to verify the impact of this study on prognosis.

Conclusions

Significant differences were observed in tumor diameter, BMI, age between the HT and TT groups. Suggests that a combination of LNM, ETE and multifocal carcinoma is a reasonable way to determine the extent of the procedure. IFS was found to be highly reliable, especially in evaluating central compartment LNM. Compared to the NCCN guidelines, our standards result in more TT being performed, and 33.33% cases who underwent TT were found to have occult contralateral cancer. The use of IFS could assist certain patients in avoiding the risk of needing a second surgery.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://gs.amegroups.com/article/view/10.21037/gs-23-182/rc

Data Sharing Statement: Available at https://gs.amegroups.com/article/view/10.21037/gs-23-182/dss

Peer Review File: Available at https://gs.amegroups.com/article/view/10.21037/gs-23-182/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://gs.amegroups.com/article/view/10.21037/gs-23-182/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of the Nanjing Drum Tower Hospital, the Affiliated Hospital of Nanjing University Medical School (No. 2021-096-02), and individual consent for this retrospective analysis was waived.

References

1. Cabanillas ME, McFadden DG, Durante C. Thyroid cancer. Lancet 2016;388:2783-95.
2. Carling T, Udelsman R. Thyroid cancer. Annu Rev Med 2014;65:125-37.
3. Wang TS, Sosa JA. Thyroid surgery for differentiated thyroid cancer – recent advances and future directions. Nat Rev Endocrinol 2018;14:670-83.
4. Haugen BR, Alexander EK, Bible KC, et al. 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. Thyroid 2016;26:1-133.
5. Haddad RI, Bischoff L, Ball D, et al. Thyroid Carcinoma, Version 2.2022, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw 2022;20:925-51.
6. Papini E, Crescenzi A, D'Amore A, et al. Italian Guidelines

for the Management of Non-Functioning Benign and Locally Symptomatic Thyroid Nodules. Endocr Metab Immune Disord Drug Targets 2023;23:876-85.
7. Hughes DT, Rosen JE, Evans DB, et al. Prophylactic Central Compartment Neck Dissection in Papillary Thyroid Cancer and Effect on Locoregional Recurrence. Ann Surg Oncol 2018;25:2526-34.
8. Chen L, Wu YH, Lee CH, et al. Prophylactic Central Neck Dissection for Papillary Thyroid Carcinoma with Clinically Uninvolved Central Neck Lymph Nodes: A Systematic Review and Meta-analysis. World J Surg 2018;42:2846-57.
9. Xing Z, Qiu Y, Yang Q, et al. Thyroid cancer neck lymph nodes metastasis: Meta-analysis of US and CT diagnosis. Eur J Radiol 2020;129:109103.
10. Hwang HS, Orloff LA. Efficacy of preoperative neck ultrasound in the detection of cervical lymph node metastasis from thyroid cancer. Laryngoscope 2011;121:487-91.
11. Liu Z, Wang R, Zhou J, et al. Ultrasound lymphatic imaging for the diagnosis of metastatic central lymph nodes in papillary thyroid cancer. Eur Radiol 2021;31:8458-67.
12. Lim YS, Choi SW, Lee YS, et al. Frozen biopsy of central compartment in papillary thyroid cancer: quantitative nodal analysis. Head Neck 2013;35:1319-22.
13. Raffaelli M, De Crea C, Sessa L, et al. Ipsilateral Central Neck Dissection Plus Frozen Section Examination Versus Prophylactic Bilateral Central Neck Dissection in Cn0 Papillary Thyroid Carcinoma. Ann Surg Oncol 2015;22:2302-8.
14. Back K, Lee J, Cho A, et al. Is total thyroidectomy with bilateral central neck dissection the only surgery for papillary thyroid carcinoma patients with clinically involved central nodes? BMC Surg 2022;22:251.
15. Kim Y, Roh JL, Song DE, et al. Risk factors for posttreatment recurrence in patients with intermediate-risk papillary thyroid carcinoma. Am J Surg 2020;220:642-7.
16. Kim HJ, Sohn SY, Jang HW, et al. Multifocality, but not bilaterality, is a predictor of disease recurrence/persistence of papillary thyroid carcinoma. World J Surg 2013;37:376-84.
17. Staubitz JI, Elmrich I, Musholt PB, et al. Targeted use of intraoperative frozen-section analysis lowers the frequency of completion thyroidectomy. BJS Open 2021;5:zraa058.
18. Abu-Ghanem S, Cohen O, Raz Yarkoni T, et al. Intraoperative Frozen Section in “Suspicious for Papillary Thyroid Carcinoma” after Adoption of the Bethesda System. Otolaryngol Head Neck Surg 2016;155:779-86.
19. Elshanbary AA, Awad AA, Abdelsalam A, et al. The diagnostic accuracy of intraoperative frozen section biopsy for diagnosis of sentinel lymph node metastasis in breast cancer patients: a meta-analysis. Environ Sci Pollut Res Int 2022;29:47931-41.
20. Feng JW, Pan H, Wang L, et al. Total tumor diameter: the neglected value in papillary thyroid microcarcinoma. J Endocrinol Invest 2020;43:601-13.
21. Yin DT, He H, Yu K, et al. The association between thyroid cancer and insulin resistance, metabolic syndrome and its components: A systematic review and meta-analysis. Int J Surg 2018;57:66-75.
22. Sargent J. Thyroid gland. BMI may predict risk of papillary thyroid cancer. Nat Rev Endocrinol 2014;10:252.
23. Park YM, Wang SG, Goh JY, et al. Intraoperative frozen section for the evaluation of extrathyroidal extension in papillary thyroid cancer. World J Surg 2015;39:187-93.
24. Sundram F, Robinson BG, Kung A, et al. Well-differentiated epithelial thyroid cancer management in the Asia Pacific region: a report and clinical practice guideline. Thyroid 2006;16:461-9.
25. Feng JW, Qu Z, Qin AC, et al. Significance of multifocality in papillary thyroid carcinoma. Eur J Surg Oncol 2020;46:1820-8.
26. Davidson HC, Park BJ, Johnson JT. Papillary thyroid cancer: controversies in the management of neck metastasis. Laryngoscope 2008;118:2161-5.
27. Gao X, Luo W, He L, et al. Predictors and a Prediction Model for Central Cervical Lymph Node Metastasis in Papillary Thyroid Carcinoma (Cn0). Front Endocrinol (Lausanne) 2021;12:789310.
28. Hong JC, Seo JW, Jang AL, et al. The utility of intra-operative frozen section for the evaluation of microscopic extrathyroidal extension in papillary thyroid carcinoma. Clin Otolaryngol 2017;42:1167-71.

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