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The prognostic value of regional lymph node metastases in patients of Guangdong Province, China with differentiated thyroid cancer

A multicenter retrospective clinical study

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Abstract

Although the prognostic value of nodal metastases in differentiated thyroid cancer remains controversial, it is of interest to evaluate and understand the different characteristics of predictive outcomes.

A multicenter retrospective study was conducted in 215 untreated patients with differentiated thyroid cancer from July 1997 to July 2015 in 4 medical centers of Guangdong Province. A total of 107 patients with nodal metastases (group A) were compared to 108 patients without metastases (group B). The 5-year disease-free survival (DFS), overall survival (OS), and postoperative complications in both groups were calculated. Variables predictive of DFS and OS were evaluated in group A.

The group A had lower 5-year DFS (69.16%, 11 months) and shorter median time of recurrence than those in group B (87.96%, 8.5 months, respectively, $P < 0.001$). The incidence of temporary hypoparathyroidism in group A is lower; whereas higher incidence of temporary unilateral vocal cord palsy, permanent hypoparathyroidism, permanent unilateral vocal cord palsy, and bilateral vocal cord palsy in group A were observed. Both univariate and multivariate analyses in group A revealed that age, pathological tumor node metastasis (pTNM) stage, and histology were related to DFS ($P < 0.05$); while pTNM stage and histology were related to OS only in univariate analyses.

Positive nodal metastases have significant prognostic value in patients with differentiated thyroid cancer in Guangdong, China and primarily reduce DFS. Moreover, patients with positive nodal metastases who are >45 years and have higher pTNM stage or follicular histology tend to have poor prognosis. Selective lymph node dissection with appropriate postoperative treatment and frequent follow-up should be accorded to these vulnerable groups of patients.

Abbreviations: ATA = American Thyroid Association, CT = computed tomography, DFS = disease-free survival, DTCs = differentiated thyroid cancers, FNAB = needle aspiration biopsy, NCCN = National Comprehensive Cancer Network, OS = overall survival, PND = prophylactic lymph node dissection, PTC = papillary thyroid cancer, RAI = radioactive iodine, Tg = thyroglobulin, TSH = thyroid-stimulating hormone, VCP = vocal cord palsy.

Keywords: differentiated thyroid cancer, Guangdong Province of China, postoperative complications, prognostic value, regional lymph node metastases

1. Introduction

Differentiated thyroid cancers (DTCs), including papillary, follicular, and Hurthle thyroid cancer, have become one of the fastest growing malignancies in the world.[1] Although DTC has been associated with better prognosis compared with anaplastic thyroid cancer, the 10-year relative survival rates for papillary, follicular, and Hurthle thyroid cancer are 93%, 85%, and 76%, respectively.[2] However, most thyroid cancer deaths are related to DTC, which account for nearly 95% of all thyroid cancers.[1]

Cervical lymph node metastases or nodal metastases are often associated with DTC, especially in papillary thyroid cancer (PTC). According to the 2014 National Comprehensive Cancer Network (NCCN) guideline of thyroid carcinoma, the prognostic value of regional lymph node metastases is still controversial.[3] Some researchers indicate the existence of difference in survival among those with and without nodal metastases (79% vs 82%),[4] whereas some researchers indicate that nodal metastases do not impact survival.[5]

Moreover, postoperative additional treatment and significant morbidity is dependent on the recurrence that is present in 20%

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of DTC patients.[6–7] The recurrence rate in node-negative patients is about 0% to 9%, while patients with clinically and ultrasound-positive node cases even have higher recurrence rates of 10% to 42%. Many studies of long-term follow-up also have supported that DTC patients with metastatic nodes have lower survival and higher recurrence rate.[8] However, the management of lymph node dissection in DTC remains controversial: prophylactic or therapeutic dissection is still with no conclusion. Owing to the contribution to prolonged overall survival (OS) and disease-free survival (DFS), therapeutic lymph node dissection for patients with clinically nodal metastases has been performed worldwide.[9] While it is still controversial to perform prophylactic lymph node dissection (PND) for clinically node-negative patients or not,[10–13] many researchers agree that PND is required for disease staging and may guide postoperative adjuvant therapy and follow-up.[14] Meanwhile, about 30% of PTC patients who underwent PND can influence the indication of postoperative radioactive iodine (RAI). Nevertheless, PND is related to higher risks for recurrent nerve palsies, hypoparathyroidism, chyle-leakage, and other postoperative complications.[15] Furthermore, additional clinical studies are needed for prognostic factors regarding DFS, OS, and postoperative complications in DTC patients, with careful precautions taken in cases with a cervical nodal metastases.

According to data from the Guangzhou Center for Disease Control and Prevention, the incidence rate of thyroid cancer has risen from 4.5/100,000 to 10.53/100,000 people within 10 years, which is an increase of 134%, and is still increasing at a speed of 14.4% annually. Thyroid cancer has become the fastest growing malignant tumor and its incidence rate is ranked the fourth in Guangzhou. Moreover, its incidence rate is 3.40 times higher in female patients.

The aim of our study is to estimate the prognostic value of nodal metastases for DTC patients in Guangdong Province. We further analyzed the characteristics predictive of DFS and OS associated with positive nodal metastases to establish better operation selections as well as postoperative managements.

2. Patients and methods

2.1. Study design and subjects

We collected the clinical records of 107 consecutive DTC patients with positive nodal metastases (group A) in Guangdong Province, China. These data were compared with those of 108 DTC patients without nodal metastases (group B). Most patients underwent total thyroidectomy, and a few patients underwent subtotal thyroidectomy or lobectomy. Central (level VI) and/or lateral (levels II, II, and IV) lymph node dissection on the affected side was performed in all cases. The nodal metastases were diagnosed by preoperative inspection (palpation, ultrasonography, computed tomography [CT], or fine needle aspiration biopsy [FNAB]) or surgical exploration/intraoperative frozen pathology and were confirmed by postoperative pathology. After surgery, all patients received thyroid-stimulating hormone (TSH) suppression therapy and/or RAI therapy, and TSH suppression was performed for all patients throughout the follow-up. None of them received external beam radiotherapy. During postoperative surveillance, we monitored the levels of thyroid hormones, TSH, thyroglobulin (Tg), and anti-Tg antibodies levels, as well as performed ultrasonography and/or emission computed tomography once to twice per year or FNAB in order to detect recurrence or metastases. The CT or magnetic resonance scan was added if necessary. If recurrence or metastases occurred, patients underwent RAI ablation therapy or/and excision of recurrence/metastases. Patients presented with distant metastases at the first admission were excluded from this study, and patients lost to follow-up were also excluded. All consecutive follow-up records were collected between July 1997 and July 2015 in 4 medical centers to reduce selection bias and information bias. All patients were reviewed during multidisciplinary team conferences that included surgical oncologists, pathologist, and medical oncologists.

This study was approved by the Ethics Committee of Zhujiang Hospital of Southern Medical University. The flow diagram for study subject screening and grouping is shown in Fig. 1.

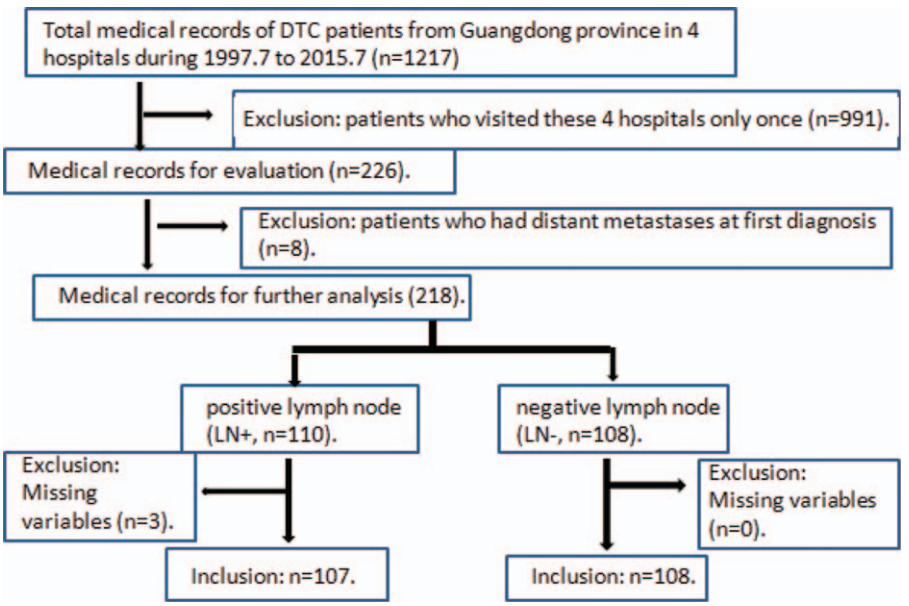

Figure 1. The flow diagram for study subject screening and grouping.

2.2. Data sources

All data were collected from follow-up medical records of patients who came from Guangdong Province from 4 medical centers in Guangzhou. The patients' demographics, surgical details, tumor status (histopathological type, tumor size, thyroidal extracapsular invasion, multifocality, and microcarcinoma), nodal metastases, pathological tumor node metastasis (pTNM) staging, postoperative complications (including transient or permanent hypoparathyroidism, transient or permanent unilateral vocal cord palsy [VCP], and bilateral VCP), distant metastases (i.e., bone, lung, kidney, brain, any other region of body, or multiorgans), and regional recurrence (thyroid and/or cervical lymph node) were recorded and analyzed.

2.3. Diagnostic criteria

The diagnostic criteria of thyroid cancer, regional recurrence, and distant metastases are determined and stratified in terms of 2014 NCCN guideline of thyroid carcinoma. Hypoparathyroidism was determined if parathyroid hormone level is <10 pg/mL (normal value = 10–65 pg/mL) and was diagnosed permanent if persisting for ≥ 6 months and requiring medical therapy. Meanwhile, VCP diagnosed by fibrolaryngoscopy was considered permanent if it persisted for ≥ 6 months. In addition, the indications for postoperative RAI were cervical nodal involvement, tumor size >1.0 cm, extracapsular thyroid invasion, unfavorable histological subtype (such as follicular, diffuse sclerosing, or tall-cell papillary cancer), and multifocal disease.

2.4. Statistical analyses

Local recurrence and/or distant metastases were the end points for DFS, while death caused by DTC was the end point for OS. All qualitative data were expressed in percentage, while quantitative data were expressed as means ± standard deviation. The statistical analyses were performed with SPSS 20.0 Software (SPSS, Inc., Chicago, IL). Pearson chi-square test was used to compare qualitative variables. Survival outcomes were analyzed using the Kaplan–Meier method. Factors related to DFS and OS in group A were analyzed using univariable and multivariable analyses. P values <0.05 were considered statistically different.

3. Results

3.1. Characteristics of cohorts

The group A consisted of 70 women and 37 men, and their mean age was 41.54 years. Group B consisted of 88 women and 20 men, and their mean age was 44.72 years. The tumor status, pTNM stage, and other details of both groups are shown in Table 1. No significant differences in age, histology, tumor size, multifocality, extrathyroidal infiltration, T stage, and 5-year OS were detected ($P > 0.05$). However, group A was associated with higher recurrent/metastatic disease than group B (31.78% vs 15.74%, respectively, $P = 0.006$). The percentage of microcarcinoma and 5-year DFS in group A (17.76% and 69.16%, respectively) were significantly lower than those in group B (34.26% and 87.96%, respectively), $P = 0.008$ and $P < 0.001$, respectively.

The incidence of postoperative complications is illustrated in Table 2. In our study, the incidence of temporary hypoparathyroidism in group B (6.48%) was higher than that in group A (3.74%); yet the incidences of temporary unilateral VCP, permanent hypoparathyroidism, permanent unilateral VCP, and bilateral VCP in group B (2.78%, 1.85%, 0%, and 0.93%, respectively) were lower than those in group A (6.54%, 8.41%, 4.67%, and 1.87%, respectively). Patients with metastases had high rate of permanent complications.

Table 1

The demographic characteristics of 2 groups.

Variables	Group A (%)	Group B (%)	P
Age, y	41.54 ± 13.30	44.72 ± 13.44	0.703
Histology			0.284
Papillary	98 (91.59%)	103 (95.37%)	
Follicular	9 (8.41%)	5 (4.63%)	
Hurthle	0 (0%)	0 (0%)	
Tumor mean size, cm	2.72 ± 1.70	2.10 ± 1.49	0.163
Multifocal	36 (33.64%)	24 (22.22%)	0.069
Microcarcinoma	19 (17.76%)	37 (34.26%)	0.008
Extrathyroidal infiltration	23 (21.50%)	24 (22.22%)	1.000
T stage			0.188
1	39 (36.45%)	50 (46.30%)	
2	27 (25.23%)	28 (25.92%)	
3	36 (33.65%)	29 (26.85%)	
4	5 (4.67%)	1 (.93%)	
N stage			
0	–	108 (100%)	–
1a	34 (31.78%)	–	
1b	73 (68.22%)	–	
pTNM stage			
1	64 (59.81%)	80 (74.07%)	–
2	0 (0%)	10 (9.26%)	
3	10 (9.35%)	17 (15.74%)	
4A	33 (30.84%)	1 (.93%)	
Recurrence/metastases	34 (31.78%)	17 (15.74%)	0.006
5-year DFS	69.16%	87.96%	<0.001
5-year OS	94.39%	96.30%	0.507

DFS = disease-free survival, OS = overall survival, pTNM = pathological tumor node metastasis.

3.2. Local recurrence and distant metastases status in both groups

Data of 17 years of follow-up are represented in Table 1, which shows 34 cases (31.78%) of recurrence/metastases in group A that was higher than that in group B (17 cases, 15.74%). The median time of recurrence/metastases in group A was shorter than that in group B (8.5 months [range: 2–62] vs 11 months [range: 3–240], respectively). Disease-specific death occurred in 6 patients in group A and 4 patients in group B. Besides, the 5-year DFS was lower in group A than in group B (69.16% vs 87.96%, respectively; $P < 0.001$). There was no difference in OS between both study groups (94.39% vs 96.30%, respectively; $P = 0.507$), which implies that DTC patients with nodal metastases in

Table 2

The comparison of postoperative complications in 2 groups.

	Group A (%)	Group B (%)
Temporary hypoparathyroidism	4 (3.74%)	7 (6.48%)
Permanent hypoparathyroidism	9 (8.41%)	2 (1.85%)
Temporary unilateral VCP	7 (6.54%)	3 (2.78%)
Permanent unilateral VCP	5 (4.67%)	0 (0%)
Bilateral VCP	2 (1.87%)	1 (.93%)

VCP = vocal cord palsy.

Table 3

Univariate analyses of factors affecting 5-year disease-free survival in group A.

Variables		Disease-free	Recurrence	Odds ratio	95% CI	*P*
Age	<45	49	15	2.35	0.18–0.98	0.045
	≥45	25	18			
Gender	Female	48	22	1.08	0.46–2.58	0.856
	Male	26	11			
T stage	1	28	11	0.99	0.64–1.54	0.972
	2	18	9			
	3	23	13			
	4	5	0			
N stage	N1a	24	10	1.10	0.45–2.68	0.827
	N1b	50	23			
pTNM stage	1	49	15	1.41	1.05–1.90	0.023
	2	0	0			
	3	8	2			
	4A	17	16			
Histology	Papillary	71	27	5.26	1.23–22.53	0.025
	Follicular	3	6			
Multifoculty	(−)	49	22	0.98	0.41–2.34	0.964
	(+)	25	11			
Microcarcinoma	(−)	61	27	1.04	0.36–3.03	0.939
	(+)	13	6			
Extrathyroidal infiltration	(−)	58	26	0.98	0.36–2.66	0.962
	(+)	16	7			

CI = confidence interval.

Guangdong can have normal life expectancy compared with those without nodal metastases.

Furthermore, age, pTNM stage, and histology were found to be associated with DFS in both univariate and multivariate analyses in group A ($P < 0.05$), whereas the gender, T stage, N stage, multifocality, microcarcinoma, and extrathyroidal infiltration were not associated with the 5-year DFS in the univariate analysis for group A ($P > 0.05$) (Tables 3 and 4). Meanwhile, the factors affecting 5-year OS in group A were pTNM stage and histology in the univariate analysis ($P = 0.034$ and $P = 0.045$, respectively) (Table 5), but this trend was not observed in the multivariate analysis (Table 6).

4. Discussion

Lymph node metastases are common in PTC, with the frequency being reported as 47% to 85% of the cases.[16–17] Metastases to central compartment nodes (level VI) frequently occur in patients with DTC.[18] In contrast, follicular cancer has a proclivity for hematogenous spread, wherein the incidence of lymph node metastases is only 9%.[19] These data are associated with treatment and follow-up. According to the 2014 NCCN guideline of thyroid carcinoma, the relationship between cervical lymph node metastases and prognosis of DTC is still controversial and needs to be more intensively examined.[3] Recent studies about long-term follow-up of nodal metastases patients show that the rate of survival was poor and associated with higher recurrence.[19] Moreover, previous studies have demonstrated several risk factors related to DTC patients with cervical node

Table 4

Multivariate analyses of factors affecting 5-year disease-free survival in group A.

Variables		Odds ratio	95% CI	*P*
Age	<45	3.00	1.19–7.53	0.020
	≥45			
pTNM stage	1	8.83	1.15–67.85	0.036
	2			
	3			
	4A			
Histology	Papillary	8.02	1.41–45.60	0.019
	Follicular			

CI = confidence interval, pTNM = pathological tumor node metastasis.

Table 5

Univariate analyses of factors affecting 5-year overall survival in group A.

Variables		Odds ratio	95% CI	*P*
Age	<45	2.62	–	0.997
	≥45			
Gender	Female	0.36	0.04–3.21	0.361
	Male			
T stage	1	0.45	0.15–1.34	0.151
	2			
	3			
	4			
N stage	N1a	0.93	0.16–5.33	0.933
	N1b			
pTNM stage	1	2.87	1.08–7.61	0.034
	2			
	3			
	4A			
Histology	Papillary	6.71	1.04–43.26	0.045
	Follicular			
Multifoculty	(−)	2.06	0.39–10.77	0.391
	(+)			
Microcarcinoma	(−)	0.92	0.10–8.38	0.943
	(+)			
Extrathyroidal infiltration	(−)	0.72	0.08–6.47	0.768
	(+)			

CI = confidence interval, pTNM = pathological tumor node metastasis.

Table 6

Multivariate analyses of factors affecting 5-year overall survival in group A.

Variables		Odds ratio	95% CI	*P*
pTNM stage	1	1.30	0.17–9.77	0.796
	2			
	3			
	4A			
Histology	Papillary	3.80	0.47–30.50	0.209
	Follicular			

CI = confidence interval, pTNM = pathological tumor node metastasis.

metastases such as age, gender, tumor size, extrathyroidal extension, tumor location, and multifocality, which can influence recurrence.[20–21] Therefore, we retrospectively investigated the prognostic value of nodal metastases in DTC patients from Guangdong Province through their natural prognoses. We also analyzed the effects of possible prognostic factors affecting DFS, OS, and postoperative complications, such as age, gender, tumor status, and pTNM stage of DTC patients with nodal metastases to assess their prognostic effects.

To explore the abovementioned controversial issues, we analyzed the data sets of 2 groups of patients with and without nodal metastases: the 5-year DFS between the 2 groups are statistically different and the recurrence or metastatic rate in group A was much higher than that in group B, but the difference of 5-year OS between 2 groups was not significant. Moreover, the recurrence/metastases occurred much earlier in group A than that in group B and primarily occurred within 5 years after the first diagnosis. Therefore, nodal metastases have poor prognostic value for DTC patients from Guangdong, and primarily influence DFS with better OS, these findings are consistent with those reported in the literature.[22] So, if nodal metastases are diagnosed preoperatively, the therapeutic cervical lymph node dissection should be carried out and may decrease recurrence rates (by up to 2%–7%) and prevent local progression into adjacent structures and improve survival (by up to 3%–9%).[23–25] Nevertheless, it should be noted that although the American Thyroid Association (ATA) guidelines recognized the importance of nodal metastases in DTC, supported only therapeutic, but not prophylactic node dissection,[26] since no benefit in terms of survival is found.[27]

Besides, in our study, the postoperative complications in the 2 groups were discrepant, and most cases of permanent complications were found in the metastatic ones. This may be because temporary complications are usually caused by temporary ischemia, while permanent complications are usually caused by intraoperative injury. In addition, patients with nodal metastases may also have hypoparathyroid or nerve violation, which increases the difficulty of operation and may cause complications. The abovementioned reasons are the primary causes of severe postoperative complications. Therefore, the therapeutic and operative plan should be considered carefully on the basis of advantages and disadvantages, and prophylactic node dissection should be avoided. The ATA guidelines also recommend central lymphadenectomy in high-risk patients but it is not considered mandatory in patients with T1 tumors.[28]

In accordance with previous research, age, gender, tumor size, nodal metastases, histology type, multifocality, microcarcinoma, extrathyroidal infiltration, and pTNM stage are considered as the primary risk factors for recurrence in DTC patients with nodal metastases in the literature.[15,29] Predominance is observed in male patients aged ≥45 years, with aggressive histotypes, capsular or locoregional infiltration, and a higher risk of locoregional and distant recurrence has been mentioned in a previous study.[30] Regarding the recurrence and/or metastases in group A in our study, we found that age, histology type, and pTNM stage were significantly associated with the 5-year DFS. Moreover, histology type and pTNM stages were significantly associated with OS only in the univariate analysis, which is slightly different from that reported in the literatures.

PTC is a unique entity in which the age at treatment is closely associated with progression and prognosis. According to recent studies, although the frequencies of nodal metastases in younger patients were more common, nodal metastases may also affect the recurrence and survival rates, particularly in older patients whose age is ≥45 years,[6] which corroborate with our results. Meanwhile, pTNM stage was an important factor for the prognosis in our study. This maybe because a patient's age affects the stage of the disease remarkably, and patients with cervical nodal metastases who are ≥45 years old are at least in stage III in the tumor node metastasis (TNM) staging system. In addition, some studies found that 80% of deaths related to DTC occur in patients aged >40 years.[19] Sugino et al[31] suggested that the incidence of distant metastases is higher in older patients and in patients with lymph node metastases. In contrast, Hughes et al showed no difference in survival related to age but showed that lymph node metastases increase the recurrence in older patients.[25,32] Through multivariate analysis, Ronga et al[33] showed that age at first admission of DTC patient is the most significantly predictive factor for time of death. Therefore, some researchers suggested that patients aged over 40 years old have crucial need for cervical lymph node dissection.[34] On the other hand, some researchers also have suggested that DTC tends to occur more frequently in patients without regard to age, which means that age is not considered as a significantly prognostic factors to DTC.[35] Still, the reason for this difference is unclear. Several hypotheses have been advocated, including the different frequency of representative gene alterations, such as *BRAF* (v-Raf murine sarcoma viral oncogene homolog B1) or *RET/PTC*.[36] In our study, age was an important prognostic factor for DFS in DTC patients with nodal metastases, and TNM staging system was also very useful for predicting the prognosis of DTC. These findings indicate the significant value of age and pTNM stage in DTC patients with nodal metastases which can help to determine the therapeutic plans, such as selecting patients to receive adjuvant RAI therapy or TSH suppression after appropriate operation and increase the frequency of postoperative follow-up.

The tumor recurrence in terms of gender still remains controversial. Previous studies suggest that thyroid cancer is more aggressive in males than in females. However, some researchers showed that gender had no significant relationship with tumor recurrence and survival.[19] In our study, the association between genders and recurrence in group A was nonsignificant. This difference may be caused due to sampling error and further prospective studies are warranted to clarify this issue.

The prognostic difference between different histologies is also a controversial issue. Some researchers have reported about poor prognosis in follicular carcinoma, but others showed that prognosis is not different in follicular carcinoma. A previous study reported that the rate of cervical nodal metastases rate at the first admission for PTC is 30%, and follicular cancer has a 9% nodal metastases rate and a 16% distant metastases rate for

its hematogenous spread.[19] In our study, both univariate and multivariate analyses showed that the recurrence and/or metastatic rates are significantly different in papillary and follicular carcinoma patients with nodal metastases. Based on this reason, the follicular type of thyroid cancer can be considered as an effective risk factor for recurrence/metastases in DTC patients with nodal metastases.

Furthermore, some literatures suggest that no correlation exists between the tumor size and nodal metastases[19]; yet, others suggest that tumor size is a prognostic factor for local recurrence.[20] Nevertheless, in our study, the tumor size was independent from recurrence in group A. This discrepancy may be associated with the different nature of study samples.

In addition, previous researches have determined that extrathyroidal invasion increases nodal metastases, and some other research has reported that the significance of extrathyroidal invasion in DTC is a prognostic indicator for local recurrence and distant metastases, and the risk of death increases by 3-fold in patients who have extrathyroidal invasion simultaneously.[19] In our study, we did not find any association between extrathyroidal invasion and recurrence/metastases in group A. This disparity may be caused by the sampling error.

Moreover, the incidence of multifocal tumors in DTC is between 22% and 88%. However, a previous study had reported no significant correlation between multifocality and prognosis,[19] which is consistent with our finding.

There are some limitations in our study. First of all, our study is susceptible to limitations associated with its retrospective nature and uncontrolled study design, hence our study has some selection and information biases. In order to reduce these biases, we collected objective records from multicenters during a long follow-up period and excluded patients who already had distant metastases at first admission. Nevertheless, some selection bias still exists in our study because it was not randomized. Second, although 2 groups were not different in most of the demographic characteristics, they were different in percentages of microcarcinoma, which may influence the homogeneity of both groups. Third, our study showed some different results compared with other studies, these disparities may be caused due to retrospective design or the different nature of samples. Fourth, our study judged nodal metastases and performed lymph node dissections based on the evidence of preoperative examination, surgical exploration, or intraoperative frozen pathology, which account for the lower sensitivity of these examinations in previous years, so it cannot be excluded that some N1a patients had subclinical lateral neck disease but were not detected at the first admission in this study, and this may underestimate the amount of N1b patients; simultaneously, some patients with potentially microscopic metastases who enrolled in our study earlier may not be excluded at the first diagnosis; thus, the final results might have been influenced. Accounting for the controversial literature results, further prospective studies are warranted. Despite these limitations, our study is unique because we investigated the natural prognosis of consecutive DTC patient series in Guangdong Province, China. In addition, the data were obtained from the natural prognosis of patients within the same race and in a relatively local region. Thus, a future prospective study in this field could shed more light on this issue.

Our study supports that nodal metastases in DTC patients significantly affect the DFS and slightly reduce the OS compared with those in patients without nodal metastases from Guangdong Province, China. In addition, the incidence of temporary postoperative hypoparathyroidism in patients without nodal metastases is higher than that in patients with nodal metastases, while the incidences of temporary unilateral VCP and permanent postoperative complications were quite opposite. Considering that cervical nodal metastases have poor prognostic value in DTC patients in Guangdong, particularly affecting DFS significantly, it is important for doctors to evaluate patients' pathological nodal status for administering better therapeutic strategies (such as choosing appropriate operation selection, postoperative treatment, and more frequent follow-up) according to patients' characteristics. When administering therapeutic strategies to DTC patients in Guangdong, there are some important aspects that have to be considered. First of all, modified radical cervical lymph node dissection should be performed when lymph node metastases are detected preoperatively or intraoperatively, so that the postoperative recurrence/metastases can be decreased as much as possible. In addition, in terms of postoperative complications, routine therapeutic lymph node dissection is preferred to PND, which could avoid increasing the rates of permanent hypoparathyroidism and of unintentional recurrent laryngeal nerve injury.[8] Furthermore, considering the recurrence and survival, routine therapeutic lymph node dissection and active postoperative therapy, such as RAI ablation, TSH suppression, and improved follow-up frequencies, are indicated in patients with nodal metastases who are aged ≥45 years, have higher pTNM stage, and aggressive histology types in order to control and prevent recurrence and/or metastases on the basis of advantages and disadvantages.

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