

## ORIGINAL ARTICLE

# Clinicopathological characteristics and prognosis of thyroid cancer in northwest China: A population-based retrospective study of 2490 patients

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## Keywords

Clinicopathological characteristic; Northwest China; prognosis; retrospective study; thyroid cancer.

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## Abstract

**Background:** The specific clinical features of thyroid cancer patients in northwest China are unclear; therefore, we analyzed the clinicopathological characteristics and prognosis of this population.

**Methods:** Clinical characteristics including age, gender, blood type, histological type, and *BRAF*<sup>V600E</sup> gene mutation; and incidence; risk factors; surgical treatment; and prognosis were recorded.

**Results:** A total of 2490 thyroid cancer patients were included; 98% were diagnosed with papillary thyroid cancer (PTC). Weight, blood type, histological type, and *BRAF*<sup>V600E</sup> gene mutation rates were significantly different. Pediatric thyroid cancer patients had higher lymph node metastasis, lower *BRAF*<sup>V600E</sup> mutation, and 6.2–9.2% greater recurrence rates than adult patients. PTC and papillary thyroid microcarcinoma displayed similar features, while in other types, such as follicular and medullary thyroid cancer, there were variations. Multiple logistic analyses showed that age (odds ratio [OR] 0.957, 95% confidence interval [CI] 0.944–0.970;  $P < 0.001$ ), focal status (OR 16.174, 95% CI 9.257–28.262;  $P < 0.001$ ), pathology (OR 0.642, 95% CI 0.473–0.871;  $P = 0.004$ ) and lymph node metastasis (OR 0.059, 95% CI 0.033–0.107;  $P < 0.001$ ) were independent factors for *BRAF*<sup>V600E</sup> mutation.

**Conclusion:** Most real world clinicopathological features, treatment, and prognosis of thyroid cancer are similar to reported data, such as the higher incidence of disease in women and the larger proportion of PTC. However, the results in pediatric patients and those with *BRAF* gene mutations are controversial and require more clinical incidence.

## Introduction

Thyroid cancer is a common malignancy of the endocrine system and occurs more frequently in women than men.<sup>1</sup> Over the past few decades, the incidence of thyroid cancer has increased in different countries, including the United States, United Kingdom, France, Canada, and Australia.<sup>2</sup> In China, the annual incidence appreciably increased by 14.51% in women during 2003–2007.<sup>3</sup> Rahib *et al.* reported that thyroid cancer will become the fourth most common cancer by 2030 in the United States if recent trends are maintained.<sup>4</sup> The burden of thyroid cancer is substantial,

thus proper preventive measures and treatment are urgently required.

Among the Chinese population, the features of thyroid cancer differ across various regions. For example, Yang *et al.* showed a gender ratio of 1:3 (1185 men: 3698 women), while Li *et al.* reported 1:3.56.<sup>5–7</sup> Other features, such as pathological distribution and *BRAF* mutations, are diverse. In this study, we investigated thyroid cancer cases in northwest China from August 2015 to June 2018 and provide information from specific areas to predict the burden of thyroid cancer in northwest China.

## Methods

### Data collection

Patients newly diagnosed with thyroid carcinoma between August 2015 and June 2018 were enrolled in the study. Clinical characteristics were collected from the thyroid database established by Xijing Hospital. Two independent researchers performed data collation and entry. In cases of disagreement, another researcher was consulted for judgment until a consensus was reached. The study was conducted in accordance with The Code of Ethics of the Declaration of Helsinki and the ethical standards of the ethics committee of Air Force Medical University. We guaranteed that the personal information of the participants was protected.

### Pathological diagnostic criteria

The pathological outcome was determined by at least two experienced pathologists from the Pathology Department of Xijing Hospital, based on standard definitions set by the World Health Organization (WHO).<sup>8</sup> Thyroid cancer was classified into papillary thyroid cancer (PTC), follicular thyroid cancer (FTC), anaplastic thyroid cancer (ATC), and medullary thyroid cancer (MTC), based on histopathological characteristics.

### Statistical analysis

Statistical analyses were performed using SPSS version 22.0 (IBM Corp., Armonk, NY, USA). A Pearson's chi-squared

( $\chi^2$ ) test was performed to determine the differences in clinicopathological factors between the groups. Continuous outcomes were analyzed using independent *t*-tests for groups of two and one-way analysis of variance among groups of three or more.  $P < 0.05$  was considered significant. Multiple logistic regression analysis was applied to identify risk factors for *BRAF*<sup>V600E</sup> mutation.

## Results

### Patients

A total of 2490 patients (1884 women: 606 men = 3.1:1) were included in the study. The average age of patients was  $43.3 \pm 11.19$  years (range: 5–80). The patients were all from northwest China, including Shaanxi, Shanxi, Xinjiang, Ningxia, and Gansu. As indicated, 98% (2440/2490) of thyroid cancer patients were identified with PTC, and more than half of these PTC patients (1295/2440) were diagnosed with papillary thyroid microcarcinoma (PTMC). Other histological types, including FTC, ATC, and MTC accounted for 0.8%, 0.04%, and 0.5%, respectively. In regard to *BRAF*<sup>V600E</sup> gene expression, 68.6% of participants were detected with the *BRAF*<sup>V600E</sup> gene and 84.5% of them showed gene mutation. The baseline features of the patients are presented in Table 1.

### Clinicopathological features of patients of different ages

To investigate the influence of patient age on clinicopathological features, we divided all patients into a children/

**Table 1** Baseline features ( $n = 2490$ )

Index	N (%)	Index	N (%)
Age		Education	
Average age	$43.3 \pm 11.19$	High school or below	1340 (53.8%)
Median age	44 (5–80)	College	1013 (40.7%)
≤ 45	1408 (56.5%)	Postgraduate and above	137 (5.5%)
> 45	1082 (43.5%)	Marriage	
Gender		Yes	2267 (91.0%)
Female	1884 (75.7%)	No	223 (9.0%)
Male	606 (24.3%)	Pathology	
Blood type		PTC	1145 (46.0%)
A	718 (28.8%)	FTC	20 (0.8%)
B	754 (30.3%)	ATC	1 (0.04%)
AB	382 (15.3%)	MTC	12 (0.5%)
O	636 (25.5%)	PTMC	1295 (52.0%)
<i>BRAF</i> detection rate	1708 (68.6%)	Others	17 (0.68%)
<i>BRAF</i> mutation		Weight (kg)	
Yes	1444/1708 (84.5%)	Average	$64.1 \pm 11.44$
No	264/1708 (15.5%)	Range	16–106

ATC, anaplastic thyroid cancer; FTC, follicular thyroid cancer; MTC, medullary thyroid cancer; PTC, papillary thyroid cancer; PTMC, papillary thyroid microcarcinoma.

adolescent group ( $\leq 20$  years old) and adult groups of various age ranges (21–45, 46–59,  $\geq 60$  years) (Table 2). Weight ( $F = 10.609$ ,  $P < 0.001$ ), blood type ( $\chi^2 = 153.656$ ,  $P < 0.001$ ), histological type ( $\chi^2 = 131.724$ ,  $P < 0.001$ ), lymph node metastasis ( $\chi^2 = 57.654$ ,  $P < 0.001$ ), surgical method ( $\chi^2 = 10.103$ ,  $P = 0.018$ ), and  $BRAF^{V600E}$  mutations ( $\chi^2 = 37.511$ ,  $P < 0.001$ ) differed among the groups. Using 45 years of age as cutoff value, we found that patients aged  $\leq 45$  weighed the least (Table 3). In regard to blood types, differences were observed between patients aged  $\leq 45$  and  $> 45$  years ( $P < 0.001$ ): 65.4% of patients aged  $\leq 45$  had A or B blood types, while 60.0% of those aged  $> 45$  years had A or O blood types. Regarding the distribution of histological types, the proportions of patients with PTC and PTMC were 51.1% versus 39.4% in the group aged  $\leq 45$ , and 47.7% versus 57.6% in the group aged  $> 45$  years, respectively. Similarly, the  $BRAF^{V600E}$  gene mutation rate in all patients was 80%, but patients aged

$> 45$  years had a 7.6% greater mutation rate than the other groups. There were no differences in the distributions of gender, lesions, lymph node metastasis, surgery method, or recurrence rate. After a medium follow-up duration of 24 months (range: 1–34), the rate of recurrence in thyroid carcinoma patients was  $\leq 10\%$ . The lung and bones were common locations for recurrence.

### Clinical features of thyroid cancer in children

In the 65 pediatric thyroid cancer patients, the ratio of girls to boys was 3.64:1. The distributions of blood type, histological type, and lesions are shown in Table 2. In contrast to adult patients, younger patients possessed higher lymph node metastasis and lower  $BRAF^{V600E}$  mutation rates (Table 2). In respect to surgical treatment, children with thyroid cancer were treated following the same guidelines

**Table 2** Characteristics of thyroid cancer patients by age group

Characteristics	< 21 (n = 65)	21–45 (n = 1343)	46–59 (n = 905)	$\geq 60$ (n = 177)	$\chi^2/F$	P
<b>Gender</b>						
Male (n = 606)	14 (21.5%)	335 (24.9%)	209 (23.1%)	48 (27.1%)	2.048	0.562
Female (n = 1884)	51 (78.5%)	1008 (75.1%)	696 (76.9%)	129 (72.9%)		
Weight	52.17 $\pm$ 13.54	63.9 $\pm$ 11.71	65.2 $\pm$ 10.61	63.12 $\pm$ 9.89	10.609	< 0.001
<b>Blood type</b>						
A (n = 718)	22 (33.8%)	401 (29.9%)	244 (27.0%)	51 (28.8%)	153.656	< 0.001
B (n = 754)	12 (18.5%)	487 (36.3%)	195 (21.5%)	60 (33.9%)		
AB (n = 382)	17 (26.2%)	198 (14.7%)	122 (13.5%)	45 (25.4%)		
O (n = 636)	14 (21.5%)	257 (19.1%)	344 (38.0%)	21 (11.9%)		
<b>Lesion</b>						
Unilateral (n = 1473)	37 (56.9%)	803 (59.8%)	540 (59.7%)	93 (52.5%)	3.661	0.3
Bilateral (n = 1017)	28 (43.1%)	540 (40.2%)	365 (40.3%)	84 (47.5%)		
<b>Histological type</b>						
PTC (n = 1145)	48 (73.8%)	671 (50.0%)	338 (37.3%)	88 (49.7%)	131.724	< 0.001
PTMC (n = 1295)	11 (16.9%)	661 (49.2%)	544 (60.1%)	79 (44.6%)		
FTC (n = 20)	5 (7.7%)	6 (0.4%)	6 (0.7%)	3 (1.7%)		
MTC (n = 12)	1 (1.5%)	4 (0.3%)	5 (0.6%)	2 (1.1%)		
Others (n = 18)	0	1 (0.1%)	12 (13.3%)	5 (2.8%)		
<b>LN metastasis</b>						
Yes (n = 1174)	59 (90.8%)	605 (45.0%)	441 (48.7%)	69 (39.0%)	57.654	< 0.001
No (n = 1316)	6 (9.2%)	738 (55.0%)	464 (51.3%)	108 (61.0%)		
<b>Surgery</b>						
Total thyroidectomy (n = 2087)	54 (83.1%)	1143 (85.1%)	733 (81.0%)	157 (88.7%)	10.103	0.018
Near-total thyroidectomy (n = 403)	11 (16.9%)	200 (14.9%)	172 (19.0%)	20 (11.3%)		
$BRAF$ detection rate (n = 1708/2490)	30/65 (46.2%)	947/1343 (70.5%)	614/905 (67.8%)	117/177 (66.1%)	18.237	< 0.001
<b><math>BRAF</math> mutation</b>						
Yes (n = 1444)	16/30 (53.3%)	778/947 (82.2%)	544/614 (88.6%)	106/117 (90.6%)	37.511	< 0.001
No (n = 264)	14/30 (46.7%)	169/957 (17.7%)	70/617 (11.3%)	11/117 (9.4%)		
Follow-up rate	56/65 (86.2%)	1200/1343 (89.4%)	759/905 (83.9%)	104/177 (58.8%)	104.978	< 0.001
<b>Recurrence</b>						
Yes	10 (15.4%)	123 (9.2%)	78 (8.6%)	11 (6.2%)	5.135	0.162
No	55 (84.6%)	1220 (90.8%)	827 (91.4%)	166 (93.8%)		

FTC, follicular thyroid cancer; LN, lymph node; MTC, medullary thyroid cancer; PTC, papillary thyroid cancer; PTMC, papillary thyroid microcarcinoma.

**Table 3** Characteristics of thyroid cancer patients aged  $\leq 45$  and  $> 45$  years

Characteristics	$\leq 45$ (n = 1408)	$> 45$ (n = 1082)	$\chi^2/F$	P
Gender				
Male (n = 606)	349 (24.8%)	257 (23.8%)	0.356	0.551
Female (n = 1884)	1059 (75.2%)	825 (76.2%)		
Weight	63.36 $\pm$ 12.63	64.86 $\pm$ 10.25	6.855	0.009
Blood type				
A (n = 718)	423 (30.0%)	295 (27.3%)	80.401	< 0.001
B (n = 754)	499 (35.4%)	255 (23.6%)		
AB (n = 382)	215 (15.3%)	167 (15.4%)		
O (n = 636)	271 (19.2%)	365 (33.7%)		
Lesion				
Unilateral (n = 1473)	840 (59.7%)	633 (58.5%)	0.339	0.561
Bilateral (n = 1017)	568 (40.3%)	449 (41.5%)		
Histological type				
PTC (n = 1145)	719 (51.1%)	426 (39.4%)	49.759	< 0.001
PTMC (n = 1295)	672 (47.7%)	623 (57.6%)		
FTC (n = 20)	11 (0.8%)	9 (0.8%)		
MTC (n = 12)	5 (0.4%)	7 (0.6%)		
Others (n = 18)	1 (0.1%)	17 (1.6%)		
LN metastasis				
Yes (n = 1174)	664 (47.2%)	510 (47.1%)	0.00	0.99
No (n = 1316)	744 (52.8%)	572 (52.9%)		
Surgery				
Total thyroidectomy (n = 2087)	1197 (85.0%)	890 (82.3%)	3.434	0.064
Near total thyroidectomy (n = 403)	211 (15.0%)	192 (17.7%)		
BRAF detection rate (n = 1708/2490)	977/1408 (69.4%)	731/1082 (67.6%)	0.95	0.33
BRAF mutation				
Yes (n = 1444)	794/977 (81.3%)	650/731 (88.9%)	18.727	< 0.001
No (n = 264)	183/987 (18.5%)	81/734 (11.1%)		
Follow-up rate	1256/1408 (89.2%)	863/1082 (79.8%)	43.044	< 0.001
Recurrence				
Yes	133 (9.4%)	89 (8.2%)	1.122	0.289
No	1275 (90.6%)	993 (91.8%)		

FTC, follicular thyroid cancer; LN, lymph node; MTC, medullary thyroid cancer; PTC, papillary thyroid cancer; PTMC, papillary thyroid microcarcinoma.

as adults. Postoperatively, 83.1% (54/65) of children underwent radioactive iodine (RAI) ablation with iodine-131 (<sup>131</sup>I) to detect metastatic disease, treat residual tumors and metastases, and to ablate any remaining normal thyroid tissue. Excluding 9 patients lost to follow-up, 10 (15.4%) patients developed recurrence, a rate 6.2–9.2% higher than in adult patients. The most common sites of recurrence were the lungs, wall of the chest, and clavicate.

### Correlation between histological type and clinical features

We analyzed the specific pathological features of each histological type, which are summarized in Table 4. As shown, 59.7% of patients with PTC had unilateral lesions, 42.6% were multifocal, 72.1% had lymph node metastasis, and 84.6% had *BRAF*<sup>V600E</sup> mutations. Similarly, in PTMC

patients, 58.1% had unilateral lesions, 51.7% were multifocal, 76.0% had lymph node metastasis, and 85.3% had *BRAF*<sup>V600E</sup> mutations. However, for other types of thyroid cancer, predominantly FTC, the clinical features were different: 76.0% of patients with PTC had unilateral lesions, 38.0% were multifocal, 24.0% had lymph node metastasis, and 42.1% had *BRAF*<sup>V600E</sup> mutations. There were no differences in local recurrence among the thyroid cancer types.

### Correlation between *BRAF* status and clinical features

More than 80% of patients had *BRAF*<sup>V600E</sup> mutations, but these occurred more often in women than in men. To investigate the relationship between clinicopathological features and *BRAF*<sup>V600E</sup> expression, all patients were divided into *BRAF*<sup>V600E</sup> positive and negative groups. As shown 5,

there were significant differences in age ( $P = 0.019$ ), lesions ( $P < 0.001$ ), focal status ( $P = 0.001$ ), histological type ( $P < 0.001$ ), and lymph nodes ( $P < 0.001$ ) between patients with or without  $BRAF^{V600E}$  mutations. Multiple logistic analyses showed that age (odds ratio [OR] 0.957, 95% confidence interval [CI] 0.944–0.970;  $P < 0.001$ ), focal status (OR 16.174, 95% CI 9.257–28.262;  $P < 0.001$ ), pathology (OR 0.642, 95% CI 0.473–0.871;  $P = 0.004$ ), and lymph node metastasis (OR 0.059, 95% CI 0.033–0.107;  $P < 0.001$ ) were independent factors for  $BRAF^{V600E}$  mutation.

## Discussion

The incidence of thyroid cancer has been steadily increasing in recent years and several studies have identified gender or racial/ethnic differences in incidence, clinicopathologic variables, gene expression, and prognosis.<sup>9–11</sup> In 2013, Rose *et al.* reported regional differences in thyroid cancer presentation and survival rates, but not within separate racial/ethnic groups.<sup>12</sup> We investigated the features of thyroid cancer in northwest China. Consistent with the results of previous reports, we found a higher incidence of thyroid cancer in

women, at a ratio of 3:1. A vast majority of patients in our sample were diagnosed with PTC, while other types, primarily FTC or MTC, accounted for only 2% of cases; contrary to our result, previous studies have indicated an incidence rate in other types of 5%.<sup>13,14</sup> Although FTC and MTC are more aggressive types, they are associated with a lower rate of lymph node recurrence. Distant metastasis was the main cause of death and the most common locations were the lungs and bones in both our study sample and in previous reports.<sup>15,16</sup>

Cancer of the thyroid gland in pediatric patients is a rare and more aggressive disease.<sup>17</sup> Patients aged  $\leq 20$  years account for 2.75% of all patients with thyroid cancer, but unfortunately the incidence appears to be increasing.<sup>18,19</sup> In this study, 2.6% (65/2490) of thyroid cancer patients were aged  $< 21$ . The low incidence and limited availability of prospective randomized trials means that there is currently a lack of evidence-based understanding of thyroid cancer in children. In 2009, Hogan *et al.* reported that in 1753 cases in children, 83% were PTC, 10% were FTC, 5% MTC, and 2% were other types.<sup>20</sup> In our sample, PTC and PTMC accounted for 90.7% of all younger patients; 7.7% and 1.5% had FTC and MTC, respectively. The same

**Table 4** Correlation between histological type and clinical features

Characteristics	PTC ( $n = 1145$ )	PTMC ( $n = 1295$ )	Other ( $n = 50$ )	$\chi^2/F$	$P$
Gender					
Male ( $n = 606$ )	308 (26.9%)	283 (21.9%)	15 (30%)	9.292	0.01
Female ( $n = 1884$ )	837 (73.1%)	1012 (78.1%)	35 (70%)		
Age					
Average	42.2 $\pm$ 11.89	44.2 $\pm$ 10.22	47.0 $\pm$ 12.93	14.1	$< 0.001$
Median	42 (5–80)	45 (13–76)	47 (8–71)		
Weight	64.8 $\pm$ 12.32	63.6 $\pm$ 10.35	62.9 $\pm$ 9.80		
Blood type					
A ( $n = 718$ )	312 (27.2%)	397 (30.7%)	9 (18.0%)	19.793	0.003
B ( $n = 754$ )	325 (28.4%)	408 (31.5%)	21 (42.0%)		
AB ( $n = 382$ )	184 (16.1%)	186 (14.4%)	12 (24.0%)		
O ( $n = 636$ )	324 (28.3%)	304 (23.5%)	8 (16.0%)		
Lesion					
Unilateral ( $n = 1473$ )	683 (59.7%)	752 (58.1%)	38 (76.0%)	6.62	0.037
Bilateral ( $n = 1017$ )	462 (40.3%)	543 (41.9%)	12 (24.0%)		
Focal					
Unifocal ( $n = 1370$ )	714 (62.4%)	625 (48.3%)	31 (62.0%)	20.596	$< 0.001$
Multifocal ( $n = 1120$ )	488 (42.6%)	670 (51.7%)	19 (38.0%)		
LN metastasis					
Yes ( $n = 1174$ )	826 (72.1%)	984 (76.0%)	12 (24.0%)	67.426	$< 0.001$
No ( $n = 1316$ )	319 (27.9%)	311 (24.0%)	38 (76.0%)		
$BRAF$ mutation ( $n = 1708$ )					
Yes ( $n = 1444$ )	644/761 (84.6%)	792/928 (85.3%)	8/19 (42.1%)	36.646	$< 0.001$
No ( $n = 264$ )	117/761 (15.4%)	136/928 (14.7%)	11/19 (57.9%)		
Recurrence					
Yes	90 (7.9%)	94 (7.3%)	4 (8.0%)	0.330	0.848
No	1055 (92.1%)	1201 (92.7%)	46 (92.0%)		

LN, lymph node.

**Table 5** Correlation between *BRAF* status and clinical features

Index	<i>BRAF</i> positive ( <i>n</i> = 1444)	<i>BRAF</i> negative ( <i>n</i> = 264)	$\chi^2/IF$	<i>P</i>
Gender				
Male ( <i>n</i> = 418)	351	67	0.139	0.71
Female ( <i>n</i> = 1290)	1093	197		
Age				
Average	44.1 ± 10.76	39.4 ± 11.60	5.547	0.019
Median	44 (14–80)	39 (6–69)		
Lesion				
Unilateral ( <i>n</i> = 1389)	1153	236	13.392	< 0.001
Bilateral ( <i>n</i> = 319)	291	28		
Focal				
Unifocal ( <i>n</i> = 919)	753	166	10.343	0.001
Multifocal ( <i>n</i> = 789)	691	98		
Histological type				
PTC ( <i>n</i> = 725)	605	120	35.7	< 0.001
PTMC ( <i>n</i> = 952)	827	125		
FTC ( <i>n</i> = 13)	5	8		
MTC ( <i>n</i> = 1)	0	1		
Others ( <i>n</i> = 7)	4	3		
LN metastasis				
Yes ( <i>n</i> = 1059)	943 (65.3%)	116 (43.9%)	43.245	< 0.001
No ( <i>n</i> = 649)	501	148		

FTC, follicular thyroid cancer; LN, lymph node; MTC, medullary thyroid cancer; PTC, papillary thyroid cancer; PTMC, papillary thyroid microcarcinoma.

guidelines for the treatment of adult patients are used to treat children with thyroid neoplasia, but these may not be appropriate.<sup>21</sup> When choosing a treatment regimen, pediatric patients undergo total or near-total thyroidectomy, considering the child's growth and the need for a second operation. Repeated radioactive iodine therapy or re-operation in cases of recurrence are reported to have negative effects on children's development. Prophylactic lymph node dissection is also debated and is not currently recommended for children.<sup>22</sup> RAI ablation with 131I is often used after surgery to detect metastatic disease, treat residual tumors and metastases, and to ablate any remaining normal thyroid tissue to allow more accurate monitoring for recurrent disease.<sup>23</sup> In our patient sample, 83.1% of children were treated with RAI ablation. However, the ideal adjuvant treatment for children with thyroid cancer following primary surgery is unclear. Moreover, it is important to note that attention should be paid to the psychological health of children with cancer. If necessary, regular psychological intervention should be considered.

*BRAF* mutations are correlated with more aggressive and iodine-resistant phenotypes and represent the most common oncogenic event in thyroid cancer, providing valuable prognostic information.<sup>24</sup> *BRAF* mutations are associated with other clinicopathological parameters, which may prove to be predictive biomarkers of therapeutic response; however, more studies are needed to confirm the viability of these potential biomarkers.<sup>25</sup> In 2012,

Kurtulmus *et al.* reported a *BRAF*<sup>V600E</sup> mutation rate of 39.45% in thyroid cancer patients.<sup>26</sup> In 2013, Fernandez *et al.* reported that *BRAF*<sup>V600E</sup> mutations occurred in 77.4% of classic PTC patients, 31.9% of the follicular variant, and 72.2% of high tall cell PTCs.<sup>27</sup> In our sample, 84.5% of patients had *BRAF*<sup>V600E</sup> mutations: 84.6% in classic PTCs, 85.3% in PTMCs, and 42.1% in the other types. These mutations were associated with age, multicentricity, histologic subtype, and lymph node metastasis. In 2013, Lim *et al.* demonstrated that *BRAF*<sup>V600E</sup> mutations were significantly associated with large tumor size, extrathyroidal extension, and lymph node metastasis.<sup>28</sup> In contrast, Ming *et al.* found no significant association between *BRAF*<sup>V600E</sup> mutations and gender, tumor size, histological subtype, multifocality, or accompanying nodular goiter and Hashimoto's; however, in thyroid cancer patients < 21 years, the *BRAF*<sup>V600E</sup> mutation rate was 53.3%, approximately 30% lower than in older patients.<sup>29</sup> By contrast, Henke *et al.* observed *BRAF*<sup>V600E</sup> mutations in 63% of pediatric thyroid cancer patients, which occurred more often in male than in female patients.<sup>30</sup> Thus, the clinical significance of *BRAF*<sup>V600E</sup> gene mutation in thyroid cancer is unresolved and more evidence is needed to establish guidelines.

The overall prognosis of thyroid cancer patients, particularly those with differentiated thyroid cancer, is excellent. Factors associated with recurrent thyroid cancer include extrathyroidal extension of the primary tumor, bulky nodal

metastatic lesions, macroscopic local invasion, and aggressive histologic subtypes.<sup>31</sup> In this study, the recurrence rates of participants in various age groups were similar at approximately 8%, except for pediatric thyroid cancer patients who had a relatively higher probability of recurrence. In 2014, Mehanna *et al.* reported a recurrence rate in PTMC patients of 7.9%.<sup>32</sup> In 2015, Joo *et al.* reported a 7.4% regional lymph node recurrence rate in PTC patients.<sup>33</sup> Meanwhile, Pedrazzini *et al.* suggested that total or near-total thyroidectomy might reduce the risk of local recurrences in non-incident PTMC, while prophylactic dissection of central compartment nodes in the absence of clinically evident metastases did not seem to change the risk of recurrence.<sup>34</sup> Moreover, RAI ablation of thyroid remnants should only be considered in young patients with multifocal tumors and histologically proven metastatic lymph nodes with a significantly higher risk of recurrence.<sup>34</sup>

In conclusion, this retrospective study revealed the real world clinicopathological features, treatment, and prognosis of thyroid cancer from a single medical center located in northwest China. Most of our results are similar to reported data, such as the higher incidence of disease in women and the larger proportion of patients with PTC. However, there is insufficient evidence to conclude which factors are associated with prognosis in pediatric patients and in patients with *BRAF* gene mutations.

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## Disclosure

No authors report any conflict of interest.

## Reference

- Cabanillas ME, McFadden DG, Durante C. Thyroid cancer. *Lancet* 2016; **388**: 2783–95.
- La Vecchia C, Malvezzi M, Bosetti C *et al.* Thyroid cancer mortality and incidence: A global overview. *Int J Cancer* 2015; **136**: 2187–95.
- Liu YQ, Zhang SQ, Chen WQ *et al.* [Trend of incidence and mortality on thyroid cancer in China during 2003–2007]. *Zhonghua Liu Xing Bing Xue Za Zhi* 2012; **33**: 1044–8 (In Chinese.).
- Rahib L, Smith BD, Aizenberg R, Rosenzweig AB, Fleshman JM, Matrisian LM. Projecting cancer incidence and deaths to 2030: The unexpected burden of thyroid, liver, and pancreas cancers in the United States. (Published erratum appears in *Cancer Res* 2014;74:4006). *Cancer Res* 2014; **74**: 2913–21.
- Wang Y, Wang W. Increasing incidence of thyroid cancer in Shanghai, China, 1983–2007. *Asia-Pac J Public Health* 2015; **27**: NP223–9.
- Yang L, Sun TT, Yuan YN, Wang N. [Time trends and pathological characteristics of thyroid cancer in urban Beijing, 1995–2010]. *Zhonghua Yu Fang Yi Xue Za Zhi* 2013; **47**: 109–12 (In Chinese.).
- Li K, Lin G, Zhou Q, Wu X. [Time trends of the incidence of thyroid cancer in urban Guangzhou, 2000–2011]. *Zhonghua Yu Fang Yi Xue Za Zhi* 2015; **49**: 142–6 (In Chinese.).
- Cameselle-Teijeiro JM, Sobrinho-Simões M. New WHO classification of thyroid tumors: A pragmatic categorization of thyroid gland neoplasms. *Endocrinol Diabetes Nutr* 2018; **65**: 133–5.
- Weeks KS, Kahl AR, Lynch CF, Charlton ME. Racial/ethnic differences in thyroid cancer incidence in the United States, 2007–2014. *Cancer* 2018; **124**: 1483–91.
- Moo-Young TA, Panergo J, Wang CE *et al.* Variations in clinicopathologic characteristics of thyroid cancer among racial ethnic groups: Analysis of a large public city hospital and the SEER database. *Am J Surg* 2013; **206**: 632–40.
- Kim J, Park WJ, Jeong KJ *et al.* Racial differences in expression levels of miRNA machinery-related genes, dicer, drosha, DGCR8, and AGO2, in Asian Korean papillary thyroid carcinoma and comparative validation using the Cancer Genome Atlas. *Int J Genomics* 2017; **2017**: 5789769.
- Rose J, Wertheim BC, Guerrero MA. Regional differences in thyroid cancer presentation and survival: A SEER study. *Endocrine Prac* 2013; **19**: 998–1006.
- Azar FK, Lee SL, Rosen JE. Medullary thyroid cancer: An update for surgeons. *Am Surg* 2015; **81**: 1–8.
- Rios A, Rodríguez JM, Parrilla P. Treatment of thyroid follicular carcinoma. *Cir Esp* 2015; **93**: 611–8.
- Jang EK, Song DE, Sim SY *et al.* NRAS codon 61 mutation is associated with distant metastasis in patients with follicular thyroid carcinoma. *Thyroid* 2014; **24**: 1275–81.
- Bansal A, Kaur M, Narula V. Cutaneous and bone metastasis of follicular thyroid carcinoma: A case report. *Tumori* 2016; **102** (Suppl 2): 103–5.
- Rivera G, Lugo-Vicente H. Thyroid cancer in children. *Bol Asoc Med P R* 2014; **106**: 48–54.
- Vergamini LB, Frazier AL, Abrantes FL, Ribeiro KB, Rodriguez-Galindo C. Increase in the incidence of differentiated thyroid carcinoma in children, adolescents, and young adults: A population-based study. *J Pediatrics* 2014; **164**: 1481–5.
- Luster M, Lassmann M, Freudenberg LS, Reiners C. Thyroid cancer in childhood: Management strategy, including dosimetry and long-term results. *Hormones (Athens)* 2007; **6**: 269–78.

- 20 Hogan AR, Zhuge Y, Perez EA, Koniaris LG, Lew JI, Sola JE. Pediatric thyroid carcinoma: Incidence and outcomes in 1753 patients. *J Surg Res* 2009; **156**: 167–72.
- 21 Francis GL, Waguespack SG, Bauer AJ *et al.* Management guidelines for children with thyroid nodules and differentiated thyroid cancer. *Thyroid* 2015; **25**: 716–59.
- 22 Raval MV, Bentrem DJ, Stewart AK, Ko CY, Reynolds M. Utilization of total thyroidectomy for differentiated thyroid cancer in children. *Ann Surg Oncol* 2010; **17**: 2545–53.
- 23 Wang L, Xiang M, Ye B *et al.* [Differentiated thyroid cancer in children: A series of 29 cases]. *Zhonghua Er Bi Yan Hou Tou Jing Wai Ke Za Zhi* 2015; **50**: 573–8 (In Chinese.).
- 24 Li DD, Zhang YF, Xu HX, Zhang XP. The role of BRAF in the pathogenesis of thyroid carcinoma. *Front Biosci (Landmark Ed)* 2015; **20**: 1068–78.
- 25 Soares P, Celestino R, Melo M, Fonseca E, Sobrinho-Simões M. Prognostic biomarkers in thyroid cancer. *Virchows Arch* 2014; **464**: 333–46.
- 26 Kurtulmus N, Duren M, Ince U *et al.* BRAF(V600E) mutation in Turkish patients with papillary thyroid cancer: Strong correlation with indicators of tumor aggressiveness. *Endocrine* 2012; **42**: 404–10.
- 27 Fernandez IJ, Piccin O, Sciascia S *et al.* Clinical significance of BRAF mutation in thyroid papillary cancer. *Otolaryngol Head Neck Surg* 2013; **148**: 919–25.
- 28 Lim JY, Hong SW, Lee YS *et al.* Clinicopathologic implications of the BRAF(V600E) mutation in papillary thyroid cancer: A subgroup analysis of 3130 cases in a single center. *Thyroid* 2013; **23**: 1423–30.
- 29 Ming J, Liu Z, Zeng W *et al.* Association between BRAF and RAS mutations, and RET rearrangements and the clinical features of papillary thyroid cancer. *Int J Clin Exp Pathol* 2015; **8**: 15155–62.
- 30 Henke LE, Perkins SM, Pfeifer JD *et al.* BRAF V600E mutational status in pediatric thyroid cancer. *Pediatr Blood Cancer* 2014; **61**: 1168–72.
- 31 Shaha AR. Recurrent differentiated thyroid cancer. *Endocr Pract* 2012; **18**: 600–3.
- 32 Mehanna H, Al-Maqbili T, Carter B *et al.* Differences in the recurrence and mortality outcomes rates of incidental and nonincidental papillary thyroid microcarcinoma: A systematic review and meta-analysis of 21 329 person-years of follow-up. *J Clin Endocrinol Metab* 2014; **99**: 2834–43.
- 33 Joo JY, Jin J, Seo ST, Lim YC, Rha KS, Koo BS. Recurrence in regional lymph nodes after total thyroidectomy and neck dissection in patients with papillary thyroid cancer. *Oral Oncol* 2015; **51**: 164–9.
- 34 Pedrazzini L, Baroli A, Marzoli L, Guglielmi R, Papini E. Cancer recurrence in papillary thyroid microcarcinoma: A multivariate analysis on 231 patients with a 12-year follow-up. *Minerva Endocrinol* 2013; **38**: 269–79.