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Outcomes and Pathological Features of Total Thyroidectomy in Patients with Multifocal Papillary Thyroid Carcinoma

Multifokal Papiller Tiroid Karsinomlu Hastalarda Total Tiroidektominin Sonuçları ve Patolojik Özellikleri

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ABSTRACT

Aim: The incidence of thyroid cancer has increased dramatically in recent decades. Multifocality is considered a poor prognostic factor for papillary thyroid carcinoma (PTC). Patients with multifocal PTC (MPTC) are at high risk for local recurrence, as well as lymphatic and distal metastases. This study examined the features and outcomes of MPTC.
Material and Methods: This retrospective study was conducted on 300 patients with PTC. Patients were classified into a multifocal group and a unifocal group. The pathological features of the PTC and the patients' outcomes were analyzed and compared.
Results: The multifocal group included 146 patients (48.7%), while the unifocal group included 154 patients (51.3%). The occurrence of multifocality was higher in females than in males (Odds ratio, OR: 2.37, 95% confidence interval, CI: 1.20-4.67, p=0.015). Tumor size of >1 cm in the multifocal group was larger than in the unifocal group (2.5 and 2.2 cm, respectively, p=0.021). Moreover, in multifocal group higher moderate risk of recurrence was detected than in the unifocal group (OR: 1.63, 95% CI: 1.01-2.60, p=0.044). At follow-up after treatment, MPTC patients had higher lymph node metastasis (OR: 2.89, 95% CI: 1.23-6.80, p=0.014). In addition, significantly higher thyroglobulin plasma levels (p=0.026) and disease recurrence (OR: 2.41, 95% CI: 1.05-5.52, p=0.037) were found in the multifocal group compared to the unifocal group.
Conclusion: Patients with MPTC had a higher risk of disease recurrence, and multifocality was concluded to be an independent prognostic factor for overall disease recurrence.
Keywords: Papillary thyroid carcinoma; thyroidectomy; multifocality; recurrence.

ÖZ

Amaç: Tiroid kanseri insidansı son yıllarda önemli ölçüde artmıştır. Multifokalite, papiller tiroid karsinomu (papillary thyroid carcinoma, PTC) için kötü bir prognostik faktör olarak kabul edilir. Multifokal PTC (MPTC)li hastalar, lenfatik ve distal metastazların yanı sıra lokal nüks açısından yüksek risk altındadır. Bu çalışmada MPTC özellikleri ve sonuçları incelendi.
Gereç ve Yöntemler: Bu retrospektif çalışma, 300 PTC'li hasta üzerinde yapıldı. Hastalar multifokal grup ve unifokal grup olmak üzere sınıflandırıldı. PTC'nin patolojik özellikleri ve hastaların sonuçları analiz edildi ve karşılaştırıldı.
Bulgular: Multifokal grupta 146 hasta (%48,7), unifokal grupta ise 154 hasta (%51,3) vardı. Multifokalite oluşumu kadınlarda erkeklerden daha yüksekti (Odds ratio, OR: 2,37, %95 güven aralığı, GA: 1,20-4,67; p=0,015). Multifokal gruptaki >1 cm olan tümör boyutu, unifokal gruptakinden daha büyüktü (sırasıyla 2,5 ve 2,2 cm; p=0,021). Ayrıca, multifokal gruptaki orta düzeyde nüks riskinin unifokal gruba göre daha yüksek olduğu saptandı (OR: 1,63, %95 GA: 1.01-2.60; p=0,044). Tedavi sonrası takipte, MPTC hastalarında daha yüksek lenf nodu metastazı vardı (OR: 2,89, %95 CI: 1,23-6,80; p=0,014). Ek olarak, tiroglobulin plazma seviyeleri (p=0.026) ve hastalık nüksü (OR: 2,41, %95 CI: 1,05-5,52; p=0,037), multifokal grupta unifokal gruba göre anlamlı olarak daha yüksek bulundu.
Sonuç: MPTC'li hastalarda hastalık nüksü riski daha yüksekti ve multifokalitenin genel hastalık nüksü için bağımsız bir prognostik faktör olduğu sonucuna ulaşıldı.
Anahtar kelimeler: Papiller tiroid karsinomu; tiroidektomi; multifokalite; nüks.

INTRODUCTION

The incidence of papillary thyroid carcinoma (PTC) has increased over the past years. That's about 5% in the last decade in the United States (1,2). These tumors comprise 80 to 85% of all thyroid cancers among people living in iodine-rich areas (3).

Multifocality is considered a poor prognostic factor for PTC (4). The prevalence of multifocal PTC (MPTC) has risen over the past decade (5,6). Patients with MPTC are at high risk for local recurrence, as well as lymphatic and distal metastases. In addition, patients with bilateral MPTC have a worse prognosis than patients with unilateral PTC (7). While patients with intrathyroidal MPTC are less likely to have a recurrence (8,9), patients with extrathyroidal MPTC have an increased risk of lymphatic metastases (10). MPTC may present as a microcarcinoma (≤10 mm) or as large tumors in two or more separate locations in the thyroid gland. Multifocal or bilateral malignant nodules are often detected after surgery in surgical specimens (11).

Fine needle aspiration biopsy (FNAB) of thyroid nodules is commonly used to detect malignancies and has a 99% accuracy (12,13). A preoperative diagnosis of MPTC may help surgeons decide on the best surgical treatment. A thyroidectomy is the standard approach to treating patients with PTC, followed by treatment with radioactive iodine (RAI; I-131) and levothyroxine therapy. Choosing an appropriate treatment can significantly reduce disease recurrence and mortality from PTC (9).

This study aimed to evaluate outcomes and pathological features of total thyroidectomy in patients with MPTC.

MATERIAL AND METHODS

Study Design and Patients

This retrospective cohort study involved patients with PTC who underwent total thyroidectomy in the thoracic ward of Imam Reza Hospital, Tabriz University of Medical Sciences, Iran. Patients were treated from January 2014 to July 2019. Patients with pathologically confirmed PTC were divided into two groups, unifocal PTC group and multifocal PTC group. The ethics committee of Tabriz Azad University of Medical Sciences approved the study proposal on 29.06.2021 with the ethics code IR.IAU.TABRIZ.REC.1400.042

Inclusion Criteria and Exclusion Criteria

Patients who had been confirmed with PTC by a pathological examination after total thyroidectomy were included in this study. Patients who had not been diagnosed with PTC and patients with different pathologic types other than classical PTC (CPTC) were excluded from this study. In addition, pregnant women and patients who underwent a hemithyroidectomy were also excluded.

Clinicopathological Variables and Follow-up

Demographic and medical data, including age, gender, underlying diseases, type of surgery, radiation exposure, family history of PTC, ultrasound (US) findings, FNAB reports, and RAI therapy, were collected for each patient. In addition, pathological parameters, including tumor size, vascular invasion, capsular invasion, extrathyroidal extension (ETE), and lymph node metastasis (LNM) were recorded according to the tumor node metastasis (TNM) staging system (9). The disease persistence at last visit and disease recurrence were evaluated according to the finding of histopathology, imaging, and thyroglobulin (Tg) levels. Negative finding of pathological evaluation and Tg level indicated the disease-free condition. Determining the response to primary treatment, disease outcome 12 months after initial treatment, and disease recurrence during follow-up was considered according to the 2015 American Thyroid Association (ATA) management guidelines (9).

Patients with an excellent response defined as no clinical, biochemical, or structural evidences of disease. Abnormal Tg values or rising anti-Tg antibodies in the absence of localizable disease was considered as incomplete biochemical response to therapy. Incomplete structural response was considered when a newly identified locoregional or distant metastases were observed. An indeterminate response was indicated by non-specific biochemical and/or structural findings that were not reliable enough to differentiate between benign or malignant responses (9).

Statistical Analysis

All demographic information and studied data were analyzed using IBM® SPSS® Statistics v.21.0 software. The mean, standard deviation, and 95% confidence interval (CI) were calculated with the quantitative variables for descriptive purposes. The chi-squared and Fisher's exact test were used for the categorical variables, and the independent t-test was considered for continuous variables. Qualitative variables were expressed as numbers and percentages. In addition, continuous variables were evaluated as mean and standard deviation or as median and interquartile ranges. An odds ratio (OR) was used to indicate the strength of the association between the risk factors and clinical outcomes. A p-value ≤0.05 was considered to be statistically significant.

RESULTS

Patient Characteristics

The study involved 300 patients with pathologically confirmed PTC who underwent a total thyroidectomy: 45 patients (15%) were male, and 255 patients (85%) were female. The demographics and characteristics of PTC patients were shown in Table 1. The mean age of the patients was 43.3±13.8 years. A family history of PTC was detected in 22 patients (7.3%). LNM was found in 136 patients (45.3%) and not found in 164 patients (54.7%); central LNM (CLNM) and lateral LNM (LLNM) were observed in 88 patients (29.3%) and 48 patients (16%), respectively. The FNAB examination results were consistent with the results of the pathological examination in 288 patients (96%). In addition, the US examination reports showed the same results as the pathological findings in 271 patients (90.3%). Before surgery, the evaluation of thyroid function showed that 291 patients (97%) were euthyroid. A total thyroidectomy was performed on 166 patients (55.3%). A dissection of the lymph nodes to remove lymph nodes in the neck was performed in 133 patients (44.3%). A total of 291 patients (97.0%) received a cumulative dose of I-131 (≤30 mCi) postoperatively. The median follow-up was 38.5 months. The Tg level of 54 patients was not measurable. However, in 246 patients Tg level measured,

the median Tg level was 0.2 (range, 0.16-1.2) IU/mL. After treatment, LNM and disease recurrent were detected in 28 patients (9.3%).

Disease Outcome 12 Months after Primary Treatment

One year after primary treatment, 281 patients (93.7%) showed an excellent response. However, 19 (6.3%) patients, including 15 females (78.9%) and 4 males (21.1%), had non-excellent responses according to the 2015 ATA management guidelines (incomplete biochemical response, incomplete structural response, and indeterminate response). Variables related to the non-excellent response after 12 months of primary treatment were shown in Table 2. These variables included the focality of disease (multifocal and unifocal), LNM, vascular invasion, ETE, distant metastasis, and tumor size.

Comparison of the Unifocal and Multifocal Groups

The comparison of the multifocal and the unifocal groups were shown in Table 3. The multifocal group included 146 patients (48.7%), while the unifocal group included 154 patients (51.3%). The mean ages in the multifocal and unifocal groups were 43.4±13.9 and 43.3±13.7 years, respectively (p=0.971). Multifocality occurred more often in females than males (OR: 2.37, 95% CI: 1.20-4.67, p=0.015). In the tumor size >1 cm, the multifocal group had a larger

Table 1. Patients' characteristics

Age (years), mean±SD	43.3±13.8
Gender (female), n (%)	255 (85%)
Gender (male), n (%)	45 (15%)
History of radiation, n (%)	2 (0.7%)
Family history, n (%)	22 (7.3%)
Diabetes, n (%)	42 (14.0%)
Hypothyroidism (follow-up), n (%)	8 (2.7%)
Hyperthyroidism (follow-up), n (%)	3 (1.0%)
Normothyroidism (follow-up), n (%)	291 (97.0%)
Ultrasound findings, n (%)	271 (90.3%)
FNAB, n (%)	288 (96.0%)
Tumor size (cm), median (IQR) [min-max]	2 (1.5-3.0) [0.3-9.0]
Tumor size (<1 cm), n (%)	39 (13.0%)
Tumor size (≥1 cm), n (%)	261 (87.0%)
LNM (CLNM and LLNM) at diagnosis, n (%)	136 (45.3%)
Multifocal disease, n (%)	146 (48.7%)
Unifocal disease, n (%)	154 (51.3%)
Capsule invasion, n (%)	164 (54.7%)
Vascular invasion, n (%)	160 (53.3%)
Extrathyroidal extension, n (%)	34 (11.3%)
Distant metastasis, n (%)	5 (1.7%)
Cervical LN dissection, n (%)	133 (44.3%)
TT surgery, n (%)	166 (55.3%)
TT + LND surgery, n (%)	14 (4.7%)
TT + CND surgery, n (%)	40 (13.3)
TT + LND + CND surgery, n (%)	79 (26.3%)
TNM stage I, n (%)	265 (88.3%)
TNM stage II, n (%)	22 (7.3%)
TNM stage III, n (%)	9 (3.0%)
TNM stage IV, n (%)	4 (1.3%)
Treatment with I-131 (ATA), n (%)	291 (97.0%)
Transient hypocalcemia, n (%)	16 (5.3%)
Vitamin D deficiency hypocalcemia, n (%)	16 (5.3%)
Persistent hypocalcemia, n (%)	1 (0.3%)
Tg level at follow-up (IU/ml), median (IQR) [min-max]	0.2 (0.18-0.23) [0.16-1.20]
Low recurrence risk (ATA), n (%)	110 (36.7%)
Medium recurrence risk (ATA), n (%)	188 (62.7%)
High recurrence risk (ATA), n (%)	6 (2.0%)
LNM (CLNM and LLNM) at follow-up, n (%)	28 (9.3%)
Recurrence of the disease, n (%)	28 (9.3%)

SD: standard deviation, IQR: interquartile range, FNAB: fine needle aspiration biopsy, LNM: lymph node metastasis, CLNM: central lymph node metastasis, LLNM: lateral lymph node metastasis, LN; lymph node, TT: total thyroidectomy, LND: lateral node dissection, CND: central node dissection, TNM: tumor node metastasis, ATA: American thyroid association, Tg: thyroglobulin

Table 2. Comparison of variables between excellent response group and non-excellent response group of patients with PTC

	Excellent Response (n=281)	Non-Excellent Response (n=19)	p
Gender (female), n (%)	240 (85.4)	15 (78.9)	0.502
Family history, n (%)	20 (7.1)	2 (10.5)	0.639
Multifocal disease, n (%)	132 (47.0)	14 (73.7)	**0.032**
Lymph node metastasis, n (%)	73 (26.0)	13 (68.4)	**<0.001**
Vascular invasion, n (%)	149 (53.0)	11 (57.9)	0.813
Extrathyroidal extension, n (%)	30 (10.7)	4 (21.1)	0.249
Distant metastasis, n (%)	4 (1.4)	1 (5.3)	0.281
Tumor size (cm), median (IQR) [min-max]	2 [0.3-9.0]	3.65 [1.5-6.0]	**<0.001**

PTC: papillary thyroid carcinoma, IQR: interquartile range, excellent response: no clinical, biochemical, or structural evidence of disease, non-excellent response: composed of incomplete biochemical, structural, and indeterminate response, definition criteria was according to the 2015 American Thyroid Association thyroid cancer guidelines

Table 3. Comparison of variables between multifocal group and unifocal group of patients with PTC

	Multifocal (n=146)	Unifocal (n=154)	p
Gender (female), n (%)	132 (90.4)	123 (79.9)	**0.015**
Age (years), mean±SD	43.4±13.9	43.3±13.7	0.971
Family history, n (%)	13 (8.9)	9 (5.8)	0.378
Diabetes, n (%)	20 (13.7)	22 (14.3)	>0.999
Hypothyroidism, n (%)	6 (4.1)	2 (1.3)	0.164
Hyperthyroidism, n (%)	1 (0.7)	2 (1.3)	>0.999
Normothyroidism, n (%)	141 (96.6)	150 (97.4)	0.744
FNAB, n (%)	139 (95.2)	149 (96.8)	0.565
Tumor size >1cm (cm), median (IQR) [min-max]	2.5 (1.8-3.9) [1.1-9]	2.2 (1.5-3.0) [1.1-6.5]	**0.021**
Tumor size ≤1 cm (cm), median (IQR) [min-max]	0.8 (0.6-1) [0.3-1.0]	1 (0.93-1) [0.5-1.0]	**0.003**
Tumor size (<1 cm), n (%)	19 (13.0)	20 (13.0)	>0.999
Tumor size (≥1 cm), n (%)	127 (87.0)	134 (87.0)	0.994
LNM at diagnosis, n (%)	82 (56.2)	54 (35.1)	**<0.001**
CLNM, n (%)	53 (36.3)	35 (22.7)	**0.011**
LLNM, n (%)	29 (19.9)	19 (12.3)	0.084
Capsule invasion, n (%)	87 (59.6)	77 (50.0)	0.095
Vascular invasion, n (%)	82 (56.2)	78 (50.6)	0.338
Extra thyroidal extension, n (%)	17 (11.6)	17 (11.0)	0.868
Distant metastasis, n (%)	4 (2.7)	1 (0.7)	0.193
Cervical LN dissection, n (%)	80 (54.8)	53 (34.4)	**<0.001**
TT surgery, n (%)	66 (45.2)	100 (64.9)	**<0.001**
TT + LND surgery, n (%)	10 (6.8)	4 (2.6)	0.102
TT + CND surgery, n (%)	25 (17.1)	15 (9.7)	0.064
TT + LND + CND surgery, n (%)	45 (30.8)	34 (22.1)	0.090
TNM I, n (%)	126 (86.3)	139 (90.3)	0.369
TNM II, n (%)	11 (7.5)	11 (7.1)	>0.999
TNM III, n (%)	6 (4.1)	3 (1.9)	0.325
TNM IV, n (%)	3 (2.1)	1 (0.7)	0.359
Treatment with I131 (ATA), n (%)	137 (45.7)	154 (51.3)	-
Transient hypocalcemia, n (%)	11 (7.5)	5 (3.2)	0.125
Vitamin D deficiency hypocalcemia, n (%)	8 (5.5)	8 (5.2)	>0.999
Persistent hypocalcemia, n (%)	1 (0.7)	0 (0.0)	-
Tg level at follow-up (IU/ml), median (IQR) [min-max]	0.2 (0.18-0.24) [0.16-0.86]	0.19 (0.18-0.2) [0.17-1.2]	**0.026**
Low recurrence risk (ATA), n (%)	44 (30.1)	66 (42.9)	**0.023**
Medium recurrence risk (ATA), n (%)	100 (68.5)	88 (57.1)	**0.044**
High recurrence risk (ATA), n (%)	4 (2.7)	2 (1.3)	0.383
LNM (follow-up), n (%)	20 (13.7)	8 (5.2)	**0.014**
CLNM, n (%)	9 (6.2)	1 (0.7)	**0.007**
LLNM, n (%)	11 (7.5)	7 (4.5)	0.334
Recurrence of the disease, n (%)	19 (13.0)	9 (5.8)	**0.037**

PTC: papillary thyroid carcinoma, SD: standard deviation, IQR: interquartile range, FNAB: fine needle aspiration biopsy, LNM: lymph node metastasis, CLNM: central lymph node metastasis, LLNM: lateral lymph node metastasis, LN: lymph node, TT: total thyroidectomy, LND: lateral node dissection, CND: central node dissection, TNM: tumor node metastasis, ATA: American thyroid association, Tg: thyroglobulin

mean tumor size than the unifocal group (2.5 and 2.2 cm, respectively, p=0.021). While in tumor size ≤1 cm, the unifocal group had a larger mean tumor size than the multifocal group (1 and 0.8 cm, respectively, p=0.003).
According to the TNM scoring system, 126 patients (86.3%) in the multifocal group and 139 patients (90.3%) in the unifocal group had stage I PTC (p=0.369). In addition, patients in the multifocal group had a more advanced stage of disease (i.e., stage III/IV) than patients in the unifocal group. According to the 2015 ATA guidelines, the moderate risk of recurrence was higher for the patients in the multifocal group than for the patients in the unifocal group (OR: 1.63, 95% CI: 1.01-2.60, p=0.044). More patients in the multifocal group had distant metastases than in the unifocal group (2.7% vs. 1.3%, p=0.383). The capsular invasion was detected in 87 patients (59.6%) of multifocal and 77 patients (50.0%) of unifocal groups (p=0.095). The vascular invasion was observed in 82 patients (56.2%) and 78 patients (50.6%) in the multifocal group and unifocal group, respectively (p=0.338). In comparing the primary treatments between groups, patients in the multifocal group underwent more cervical LN dissections than in the unifocal group (54.8% and 34.4%, respectively, OR: 2.30, 95% CI: 1.45-3.67, p<0.001). After treatment, LNM, particularly CLNM, occurred more frequently in patients in the multifocal group than in the unifocal group (OR: 2.89, 95% CI: 1.23-6.80, p=0.014 for LLNM, and OR: 10.05, 95% CI: 1.25-80.36, p=0.007 for CLNM). The median level of plasma Tg in the multifocal group was meaningfully elevated compared to the unifocal group (0.2 vs. 0.19, p=0.026). Recurrence of the disease in the multifocal group was significantly higher than in the unifocal group (OR: 2.41, 95% CI: 1.05-5.52, p=0.037).

DISCUSSION

PTC is the most common type of well-differentiated thyroid cancer. Multifocality is related to an increased risk of recurrence of PTC. However, its prognostic value in clinical outcomes is controversial. Choi et al. (14) performed a retrospective study on 2,390 patients with pathologically confirmed PTC. They found that multifocal tumors were an independent risk factor for the recurrence of PTC after total thyroidectomy. Geron et al. (15) studied the data of patients with PTC from tertiary medical centers. They analyzed the main characteristics of PTC as well as patient outcomes in order to evaluate prognostic implications in MPTC patients. In their study, the median follow-up of patients was 10.1 years. MPTC was detected more frequently than unifocal PTC, and often presented in older patients and more frequently in males. MPTC was also associated with higher LNM involvement, more advanced stages (III/IV), a higher risk of recurrence according to the ATA, more recurrence during follow-up, and higher overall mortality rates. However, the researchers concluded that multifocality was not an independent prognostic factor for long-term outcomes. In addition, 78.3% of all patients showed excellent response, 1 year after treatment. Patients in the unifocal group had a higher percentage of excellent response compared to patients in the multifocal group. After 12 months of initial treatment, worse response to the treatment was associated with multifocal disease, the male gender, a large tumor, advanced TNM stage, a high risk of recurrence, ETE, LNM, and distant metastases. In a retrospective review on patients with PTC who underwent thyroid surgery (10), patients with MPTC were older, had a smaller average tumor size, presented an advanced TNM stage and had a higher rate of non-remission and a lower survival rate than patients with unifocal PTC. Within a mean follow-up of 7.1±5.3 years, 25 patients with MPTC (4%) died.
In our study, a total thyroidectomy was performed in all patients and the median follow-up was 38.5 months. MPTC affected more females than males. The age of most of the patients was 43.3±13.8 years old. In addition, patients in the multifocal group had an advanced level of disease (stage III/IV), a higher rate of distant metastasis, and a higher moderated recurrence risk than patients in the unifocal group. Furthermore, patients with a large tumor, multifocal disease, LNM, vascular invasion, and ETE did not have an excellent response after treatment.
The approaches for diagnosing and treating recurrent PTC are different from the management strategies for primary thyroid tumors. Tg is a tumor marker that is used for the follow-up of thyroid cancers (16). Patients with tumor recurrence after surgery are expected to have high levels of Tg (16,17). During the follow-up of PTC patients after surgery, we found that patients with MPTC had higher plasma levels of Tg than patients with unifocal PTC.
Kuo et al. (6) investigated the clinical features and therapeutic outcomes of multifocal papillary thyroid microcarcinoma (PTMC) in patients with PTC who had undergone a thyroidectomy at one medical center. More patients in the multifocal PTC group had stage I than in the non-PMTC group: 63.1% versus 56.8%. In addition, patients with multifocal PTMC had higher postoperative Tg levels. Patients in the non-PMTC group had larger tumors (2.6±0.1 cm) than in the MPTC group (2.2±0.1 cm) and showed a higher rate of postoperative disease progression than patients with PTMC. There was no statistical difference in disease-specific mortality and total mortality between patients with PTMC and non-PTMC.
Gur et al. (18) reviewed the documents of patients with PTC who underwent total or near-total thyroidectomies. Patients were classified into multifocal or unifocal groups. The researchers found that age, gender, the sizes of the tumors, ETE, and capsular invasion were statistically similar in both groups. LNM was also more common in the multifocal group than unifocal. Our data showed significantly high rates of LNM in patients in the multifocal group. We also found higher rates of capsular invasion and vascular invasion in the multifocal group than in the unifocal group. However, differences in capsular invasion and vascular invasion were not statistically significant. Moreover, we detected a significant disease recurrence in patients in the multifocal group than in the unifocal group. In addition, the median size of the tumor (>1 cm) in patients in the multifocal group was larger than patients in the unifocal group.

Limitations

In this retrospective study, we had some limitations. The first is that some patients did not meet the treatment criteria, for example, a few patients did not receive a postoperative dose of I-131 for residual tumor ablation. The second, approaches to the treatment of patients with PTC is a dynamic process, and the classification of the

disease stage, follow-up methods, and definitions of the persistent or recurrent disease can be changed over time. Furthermore, the mortality rate is low in PTC patients; consequently, we need a more population-based study to examine the relationship between multifocality and mortality.

CONCLUSION

MPTC affected more females than males and most patients with MPTC were young to middle-aged. Patients with MPTC had larger tumors and higher rates of LNM, capsular invasion, and vascular invasion than patients with unifocal PTC. Patients in the multifocal group were more likely to have recurrent disease and not to have excellent responses to treatment. Total thyroidectomy with lymph node dissection may be effective in reducing the rate of postoperative disease progression in patients with MPTC.

Ethics Committee Approval: The study was approved by the Research Ethics Committee of Tabriz Azad University of Medical Sciences (29.06.2021, 1400.042).

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