



RESEARCH

EVALUATION OF PROGNOSIS AND RISK FACTORS OF DIFFERENTIATED THYROID CANCER IN A GERIATRIC POPULATION

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ABSTRACT

Introduction: This retrospective study aimed to investigate the clinical and pathological features of differentiated thyroid cancer and to evaluate treatment outcomes in older adults.

Materials and Methods: Data from 1077 patients with differentiated thyroid cancer were noted. These patients were divided into two groups, aged < 65 years and aged ≥ 65 years, and the clinicopathological features of each were compared.

Results: Of the 1077 patients, 913 (85%) were under 65 years of age and the remaining 164 (15%) were aged ≥ 65 years. Of those aged < 65 years, 652 (71.4%) had papillary thyroid carcinoma and 261 (28.6%) had follicular thyroid carcinoma. Of the patients aged ≥ 65 years, 116 (70.7%) had papillary thyroid carcinoma and 48 (29.3%) had follicular thyroid carcinoma. The primary tumour size was significantly larger and the incidences of vascular invasion, lymph node metastasis, and distant metastasis were significantly higher in patients aged ≥ 65 years than in the younger patients ($p < 0.001$, $p < 0.001$, $p = 0.001$, and $p = 0.002$, respectively). There was no noteworthy difference between the two groups in terms of the number of tumours, tumour bilaterality, multifocality, and extravascular invasion ($p = 0.860$, $p = 0.590$, $p = 0.404$, and $p = 0.110$, respectively).

Conclusion: Primary tumour size was significantly larger and the incidences of vascular invasion, lymph node metastasis, and distant metastasis were significantly higher in patients aged ≥ 65 years. Older patients with differentiated thyroid cancer have worse pathologic features at the time of diagnosis therefore need more aggressive treatment such as more frequent and higher doses of radioiodine treatment.

Keywords: Thyroid Neoplasms; Thyroid Cancer, Papillary; Adenocarcinoma, Follicular; Neoplasm Metastasis; Geriatrics..



INTRODUCTION

Differentiated thyroid cancers (DTC) constitute 80–90% of all thyroid cancers (1). There are several factors associated with a favourable prognosis for differentiated thyroid cancer: age, tumor size, tumor stage, histologic subtype, absence of distant metastasis and response to radioiodine treatment (2). Age plays an important role in prognosis of DTC. Generally, younger patients (less than 45 years old) with DTC tend to have a better prognosis than older patients (over 45 years old).

Several studies have shown that younger patients with DTC have a lower risk of disease recurrence and mortality compared to older patients. This may be due to differences in tumor biology and the immune response to the tumor between age groups. In addition, younger patients may be more likely to receive aggressive treatment and have better overall health, which can also contribute to a better prognosis.

Age is an important factor for DTC. In the TNM classification for thyroid carcinoma, age was included as a prognostic factor, and the cut-off age was 45 years. Several publications compared survival between the two groups (i.e., patients younger and older than 45 years) (3–5). However, discussions regarding higher age limits are ongoing (6–8).

In particular, it is known that thyroid cancer incidence increases with age, with a peak incidence in the 6th and 7th decades of life. Despite this, there is limited research comparing the clinic and pathologic differences of DTC between young and old patients.

This study aims to investigate the clinic and pathologic characteristics of DTC in young and old patients, with a focus on identifying any differences in tumor characteristics and disease progression. By understanding the unique features of DTC in different age groups, clinicians can better tailor their management strategies and improve the overall care of patients with this disease.

MATERIALS AND METHODS

A total of 1077 patients with DTC registered in Başkent University Ankara Hospital outpatient clinic of Endocrinology from 2011 to 2021 were identified and retrospectively analysed.

Patients were divided into two groups based on ages, those aged < 65 years and those aged ≥ 65 years. The pathological and clinical features of the two groups were compared. Information about age, gender, body mass index (BMI), diabetes, hypertension, coronary artery disease (CAD), and cancer history were evaluated. These two groups were compared in terms of tumour size, tumour multifocality, bilaterality, tumour invasion (extracapsular and vascular invasion), lenf node (LN) metastasis, and distant metastasis. TNM staging was performed. Recurrence and mortality from any cause were also evaluated. Recurrence was defined as detection of a tumor in the thyroid bed, cervical lymph nodes or in distant organs.

Statistical analysis

All statistical analysis was performed using SPSS for Windows v16.0 (Statistical Package for Social Sciences) package program. Continuous data were presented as means ± standard deviation. Comparisons of various numeric parameters among groups were analyzed with the students t test. Comparisons of categorical parameters among groups were analyzed with pearson chi square test. Statistical significance was set at $p < 0.05$.

RESULTS

Overall 1077 patients with differentiated thyroid cancer was analysed. Of these, 913 (85%) patients were aged < 65 years, and the remaining 164 (15%) patients were aged ≥ 65 years. The demographic and clinical characteristics of patients are shown in Table 1.

Table 1. Demographic and clinical characteristics of patients diagnosed with DTC.

Variable	< 65 y (n=913)	≥ 65 y (n=164)	P $_{\alpha,\beta}$ value
Gender (female%)	701(76.8)	115(70.1)	0.067
Age, years*	44.7±11.6	71.8±6.0	<0.001
BMI, kg/m ² *	28.16±5.34	28.26±5.45	0.691
Comorbidities			
Diabetes (%)	151(16.5)	46(28)	<0.001
Arterial Hypertension (%)	152(16.6)	49(29.9)	<0.001
Dyslipidemia (%)	89(9.7)	21(12.8)	0.234
CAD(%)	71(7.8)	23(14)	0.009
History of cancer (%)	22(2.4)	25(15.2)	<0.001

*:Mean ± Standard Deviation, BMI: Body Mass Index, CAD: Coronary Artery Disease, α : p for Age and BMI: Difference between groups student's t test, β : p for comorbidities and gender: Difference between groups Chi-square test.

Of the patients aged < 65 years, 652 (71.4%) had PTC and 261 (28.6%) had follicular thyroid carcinoma. Of those aged > 65 years, 116 (70.7%) had PTC and 48 (29.3%) had follicular thyroid carcinoma. The primary tumour size was significantly larger (1.37±0.99 cm for the patients aged < 65 years and 1.86±1.59 cm for aged ≥65 years, p<0.001). The incidences of vascular invasion (22% vs 37.8%, p<0.001,) lymph node (16.9% vs 27.4%, p=0.001) metastasis, and distant metastasis (2.3% vs 6.7%, p=0.002) were significantly higher in patients aged >65 years than in younger patients.

The percentage of distant metastasis within patients having papillary thyroid carcinoma was 0.25% and within patients having Follicular thyroid carcinoma was 0.42%. The percentage of lymph node metastasis within patients having papillary thyroid carcinoma was 17% and within patients having Follicular thyroid carcinoma was 22%.

There was no significant difference between the two groups in terms of the number of tumours (1.97±1.18 in the group of patients aged <65 years and 1.93±1.28 for aged ≥65 years, (p=0.860)). In terms of multifocality, results do not indicate

any remarkable difference (26.4% of patients aged <65 years and 24.4% of patients aged ≥65 years, p=0.590)). Similarly, there was no significant difference in percentage of patients within these two different age groups (21.2% and 18.3%, p=0.404) when bilaterality is considered. Extravascular invasion results indicated no remarkable difference (22.9% and 28.7%, p=0.110). All pathological features of the patients diagnosed with DTC are presented in Table 2.

When TNM Staging was performed, 42% of the patients in the geriatric patient group (65 years and older) were found to be in stage 4. The proportion of stage 4 patients under the age of 65 years was only 17%.

All of the patients had total thyroidectomy. The number of patients who underwent central lymph node dissection was significantly higher in those aged ≥ 65 years (p=0.039). The rate of lateral lymph node dissection was alike in both the groups (p=0.158).

The proportion of patients who underwent radioactive iodine treatment, and the dosing amount were significantly higher in patients aged ≥ 65 years



Table 2. Pathology results of patients diagnosed with DTC.

Variable	< 65 y (n=913)	≥ 65 y (n=164)	P $_{\alpha,\beta}$ value
Papillary thyroid carcinoma (%)	652(71.4)	116(70.7)	0.859
Follicular thyroid carcinoma (%)	261(28.6)	48(29.3)	0.859
Primary tumor size, cm*	1.37±0.99	1.86±1.59	<0.001
Number of tumors*	1.97±1.18	1.93±1.28	0.860
Multifocality (%)	241 (26.4)	40 (24.4)	0.590
Bilaterality (%)	193 (21.2)	30 (18.3)	0.404
Vascular invasion (%)	201 (22)	62 (37.8)	<0.001
Extracapsular invasion (%)	209 (22.9)	47(28.7)	0.110
LN metastasis (%)	154 (16.9)	45 (27.4)	0.001
Distant metastasis (%)	21(2.3)	11(6.7)	0.002

*: Mean ± Standard Deviation, LN: Lymph Node, α : p for primary tumor size and number of tumors: Difference between groups student's t test, β : p for papillary and follicular thyroid carcinoma, multifocality, bilaterality, vascular invasion, extracapsular invasion, LN and distant metastasis: Difference between groups Chi-square test.

($p < 0.001$ and $p < 0.001$, respectively). The recurrence rates were similar in both groups ($p = 0.425$). The all-cause mortality rate was significantly higher in patients than in those aged < 65 years ($p < 0.001$).

There was no difference in terms of tumour size, vascular invasion, lymph node metastasis, and distant metastasis between patients aged 65–75 years and those aged 75 years and above. Extracapsular spread was more common in patients aged 75 years and above than in patients aged 65–75 years. The recurrence rate was similar in both groups; however, as expected, the rate of all-cause mortality was higher in patients aged 75 years and above.

DISCUSSION

Age has been recognized as an important prognostic factor in DTC. This may be due to the fact that younger patients tend to have less aggressive disease and better overall health, which may enable them to tolerate more aggressive treatments and

have a better response to treatment. Our study demonstrated worse histopathological features as determinants of worse prognosis in elderly.

In this study we found larger tumor size and higher incidence of vascular invasion, lymph node metastasis and distant metastasis in patients aged ≥ 65 compared to younger patients. There was not any difference in terms of these conditions between ages 65-75 and above 75.

Tumor size is an important prognostic factor in patients with DTC and the size of the primary tumor in differentiated thyroid carcinoma may be a crucial factor in determining their likelihood of developing extrathyroidal extension, lymph node spread, and distant metastasis. Compared to patients aged < 65 years, geriatric patients had significantly higher incidences of vascular invasion, LN metastasis, and distant metastasis, which might be due to the late diagnosis of the patients (9). Some patients with PTC have poor outcomes depending on factors such as sex, tumour size, LN metastasis, presence

of extrathyroidal tissue infiltration, completeness of resection, and age at diagnosis (10). Certain studies have shown that DTCs in elderly tend to have a worse prognosis depending on larger tumor size, extrathyroidal extension and lymph node involvement at the time of diagnosis (11).

In one study, patients over 75 years of age had larger tumor size and higher tumor count than patients under 65 years of age and those aged 65–75 years. Advanced stage of tumor and metastasis (TNM) and probability of extracapsular invasion were higher compared to patients under 65 years of age and 65–75 years old (12). In our study, no difference was observed between patients aged 65–75 years and patients aged 75 years and above in terms of tumour size, vascular invasion, lymph node metastasis, and distant metastasis.) Extracapsular spread was more common in patients aged ≥ 75 years than in patients aged 65–75 years. In another study, older adults with papillary thyroid microcarcinoma were found to have more aggressive biological features and a higher recurrence rate, and it was reported that more aggressive treatment and strict follow-up could be considered in geriatric patients with a tumour diameter >5 mm (13). These more aggressive pathologic features connected to age may be related in diagnostic delay in elderly (14).

In our study there was no difference in frequency of variants of pathologic thyroid cancer. Some studies suggested relative increase in more histopathological subtypes of thyroid cancer in elder patients is related with worse prognosis (15).

Despite worse histopathologic features in our elder group, local recurrence rate was similar with young group. This is probably due to the fact that these patients treated more intense according to their worse pathologic characteristics. In our study all patients had total thyroidectomy, though central lymph node dissection was higher in older patients. We also found more frequent and more intense radioiodine treatment in elderly. The number

of patients who underwent central lymph node dissection was significantly higher in those aged ≥ 65 years ($p=0.039$). The rate of lateral lymph node dissection was alike in both the groups ($p=0.158$). In addition, one study found no significant difference in central and lateral neck dissections performed in elderly and young patients (9). Another study indicated that patients in the elderly group were more likely to show central compartment lymph node metastasis (CLNM) ($p<0.010$), especially the ratio of CLNM >0.5 ($p<0.010$), more than patients <65 years of age (13), which was in line with our study.

There are some limitations of our study. First of all, retrospective design of our study is a major limitation. We did not investigate the side effects of more aggressive treatment in older patients. Further prospective studies are needed to decide most appropriate treatment approach in older population.

In conclusion, older patients with differentiated thyroid cancer have worse pathologic features at the time of diagnosis therefore need more aggressive treatment such as more frequent and higher doses of radioiodine treatment.

CONCLUSION

In conclusion, this study revealed that the primary tumour size was significantly larger and the incidences of vascular invasion, lymph node metastasis, and distant metastasis were significantly higher in patients aged ≥ 65 years. Older patients with differentiated thyroid cancer have worse pathologic features at the time of diagnosis therefore need more aggressive treatment such as more frequent and higher doses of radioiodine treatment.

Conflict of interest

The authors state that there is no conflict of interest.



Ethics approval

This was a retrospective study. This study has an approval from Başkent University Institutional Review Board (KA21/497, Project Number) and supported by Başkent University Research Fund.

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