Original Article

A Study of Clinicopathologic Features of Thyroid Cancer in Western Iran: A 9-Year Experience

Babak Izadi, Somayeh Jalilian[1], Mazaher Ramezani, Masoud Sadeghi[2], Sedigheh Khazaei

Molecular Pathology Research Center, Imam Reza Hospital, Kermanshah University of Medical Sciences, [1]Students Research Committee, Kermanshah University of Medical Sciences, [2]Medical Biology Research Center, Kermanshah University of Medical Sciences, Kermanshah, Iran

Abstract

Introduction: Thyroid cancer is reported as the most rapidly increasing and third-most common cancer among females. This study aimed to evaluate the data related to thyroid cancer in Kermanshah, Iran, for the first time. **Materials and Methods:** The data of thyroid cancers were obtained between March 2008 and March 2017. Tumors were classified into four groups: papillary, follicular, medullary, and anaplastic; age was divided into two groups (<45 years and ≥45 years); and tumor size was divided into three groups (≤2, 2–4, and >4 cm) according to the National Comprehensive Cancer Network guidelines for patients: Thyroid cancer, version 1, 2017. **Results:** A total of 296 thyroid cancer patients with the mean age of 41.1 years, 75% of whom were female, were studied. Most patients (89%) had papillary thyroid cancer. Of all patients, 8.8%, 21.3%, 20.6%, 27%, 5.7%, and 16.9% of patients had extrathyroidal invasion, lymph node metastasis, capsular invasion, Hashimoto's thyroiditis, distant metastasis, and goiter, respectively. With regard to the stage, 82.4% of patients had Stage I. There were significant differences between the two genders in the mean age and Hashimoto's thyroiditis. There were significant differences between the two age groups in sex and Hashimoto's thyroiditis. In addition, there were significant differences between tumor size group and laterality and vascular invasion. **Conclusions:** The mean age and female/male ratio in this study were similar to those of other areas of Iran. Papillary thyroid carcinoma is the most common kind of thyroid cancer in Iran. In addition, more attention should be paid to the role of Hashimoto's thyroiditis in Iranian patients with thyroid cancer in the future.

Keywords: *Iran, prevalence, thyroid cancer*

Introduction

Cancer is a major public health problem in the world and has remained one of the leading causes of death in many countries.[1] Thyroid cancer is the most common malignancy of endocrine system with an incidence continuing to increase in the recent decades.[2] According to data recorded, more than 213,000 new cases of thyroid malignancy are registered annually in the world, causing approximately 35,000 deaths each year.[3] The incidence rate of thyroid carcinoma is estimated to be 2.20/100,000 people/year in Iran.[3] Thyroid cancer is reported as the most rapidly increasing and third-most common cancer among women.[4-6] Women are affected more frequently than men, with ratios of 2:1–4:1.[7] The type of tumor is an important prognostic factor for thyroid carcinoma. Papillary thyroid carcinoma (PTC), follicular thyroid carcinoma (FTC), medullary thyroid carcinoma (MTC), and anaplastic thyroid carcinoma (ATC) are pathological subtypes of thyroid cancer. Thyroid cancers have remarkably different features.[8] PTC is the most common kind of thyroid cancer.[8] PTC accounts for nearly 80% of all thyroid malignancies.[9] PTC is able to metastasize to the lymph nodes (LNs) during the early stages of the disease, and nodal metastasis can consequently increase the cancer-specific mortality and locoregional recurrence rates.[10,11] FTC is the second-most common type of thyroid malignancy that accounts for nearly 20% of all thyroid cancers. The 10-year disease-specific survival of patients with FTC has been found to be 85%–92% in retrospective series.[11] MTC constitutes 5% of thyroid cancers; however, it causes 13% of all thyroid cancer-related deaths. There has been an increase in the incidence of MTC over the past 30 years with a diagnosis of smaller tumors.[12] ATC is more rare and accounts for <5%

How to cite this article: Izadi B, Jalilian S, Ramezani M, Sadeghi M, Khazaei S. A study of clinicopathologic features of thyroid cancer in Western Iran: A 9-year experience. Clin Cancer Investig J 2019;8:64-9.

Address for correspondence:
Dr. Mazaher Ramezani, Molecular Pathology Research Center, Imam Reza Hospital, Kermanshah University of Medical Sciences, Kermanshah, Iran.
E-mail: mazaher_ramezani@yahoo.com

Access this article online

Website: www.ccij-online.org

DOI: 10.4103/ccij.ccij_7_19

Quick Response Code:

of all thyroid tumors, but more than 50% of all thyroid cancer deaths with 93.5 days' survival occurs in a series of 34 patients.[13] Histopathologic subtypes of thyroid cancer have been shown to differ in clinical features and genetic determinants. Epidemiological features of thyroid cancer are important to clinicians. Thyroid cancer shows considerable ethnic and geographic variation and has not revealed consistent patterns. Furthermore, the pathologic characteristics of tumors are important. Pathologic diagnosis can help in primary treatment, better planning for prevention, and further studies. The study aimed to determine the epidemiology and clinicopathologic characteristics of thyroid cancers in the west of Iran which will help clinicians developing better diagnostic and therapeutic modalities. The aim of this study was performed to provide the data related to thyroid cancer in Kermanshah, Iran (a city located in the west of Iran), for the first time.

Materials and Methods

This study was approved by the Ethics Committee of Kermanshah University of Medical Sciences, Kermanshah, Iran. The data were obtained from the thyroid cancer patients admitted between March 2008 and March 2017. All cases were enrolled in this study from Imam Reza Hospital in Kermanshah, Iran. This hospital is the main training center of pathology in the west of Iran. Histological reports were screened for thyroid cancers. Various clinicopathologic and prognostic factors were described in this study such as pathologic type of the thyroid cancer, age, gender, tumor size, extrathyroidal extension, laterality, and LNs status. Tumors were classified into four groups: papillary, follicular, medullary, and anaplastic; age was divided into two groups (<45 years and ≥45 years); and tumor size was divided into three groups (≤2, 2–4, and >4 cm). These divisions were done based on the National Comprehensive Cancer Network (NCCN) guidelines for patients: thyroid cancer, version 1, 2017 (available online at NCCN.org/patients).

The data were analyzed by SPSS software (version 22.0, IBM Corp., Armonk, NY, USA) using *t*-test and Chi-square test to compare quantitative/numeric and qualitative/categorical variables, respectively. $P < 0.05$ was considered to be statistically significant.

Results

A total of 296 thyroid cancer patients with the mean age of 41.1 years (range, 1–93 years), 75% of whom were female, were studied [Table 1]. Most patients (89%) had papillary thyroid cancer. The mean tumor size in the patients was 2.2 cm (range, 0.1–16 cm). Among all patients, 8.8%, 21.3%, 20.6%, 27%, 5.7%, and 16.9% had extrathyroidal invasion, LN metastasis, capsular invasion, Hashimoto's thyroiditis, distant metastasis, and goiter, respectively. With regard to the stage, 82.4% of patients had Stage I, followed by Stages II, III, and IV. The right side had the highest laterality in the patients (54.1%), followed by the left side, and bilateral tumor. Among 263 patients, 11%

Table 1: Characteristics of the patients with thyroid cancer (*n*=296)

Variable	Value
Age, year	
Mean±SD	41.1±14.9
Range	1-93
Sex (%)	
Male	74 (25)
Female	222 (75)
Histological type	
Papillary	263 (89)
Follicular	24 (8)
Medullary	5 (1.7)
Anaplastic	4 (1.3)
Tumor size, cm	
Mean±SD	2.2±2.1
Range	0.1-16
Extrathyroidal invasion (%)	
Positive	26 (8.8)
Negative	270 (91.2)
Lymph node metastasis (%)	
Positive	63 (21.3)
Negative	233 (78.7)
Stage (%)	
I	244 (82.4)
II	30 (10.1)
III	16 (5.4)
IV	6 (2)
Capsular invasion (%)	
Positive	61 (20.6)
Negative	235 (79.4)
Hashimoto's thyroiditis (%)	
Positive	80 (27)
Negative	216 (73)
Distant metastasis (%)	
Positive	17 (5.7)
Negative	279 (94.3)
Laterality (%)	
Bilateral	31 (10.5)
Right	160 (54.1)
Left	105 (35.5)
Vascular invasion (%)	
Positive	48 (16.7)
Negative	239 (83.3)
Missing	9
Follicular variant of papillary carcinoma (*n*=263), *n* (%)	
Positive	29 (11)
Negative	234 (89)
Goiter (%)	
Positive	50 (16.9)
Negative	246 (83.1)

SD: Standard deviation

had follicular variant, and among 287 patients, 16.7% had vascular invasion.

The distributions of age and tumor size among patients with thyroid cancer are shown in Figure 1. Most patients were in the age range of 20–40 years and had the tumor size of ≤2 cm.

Table 2 presents the comparison of variables between male and female patients. There were significant differences between the two genders in the mean age (P = 0.020) and Hashimoto's thyroiditis (P = 0.016). The mean age was higher in male patients than in female patients, and the prevalence of Hashimoto's thyroiditis was higher in the female patients than in the male patients.

The comparison of some variables based on the age group (<45 years vs. ≥45 years) is shown in Table 3. There were significant differences between the two age groups in sex and Hashimoto's thyroiditis. The prevalence of male patients was higher in the age group ≥45 years than the age group <45 years. In addition, the prevalence of Hashimoto's thyroiditis was higher in the age group <45 years than the age group ≥45 years.

Tumor size was divided into three groups (≤2 cm, 2–4 cm, and >4 cm). Table 4 shows the comparison of some variables between these groups. The prevalence of bilateral tumor in size ≤2 cm was the lowest, followed by the right side in size 2–4 cm and the left side in size >4 cm (P = 0.043). In addition, the prevalence of vascular invasion was the lowest in size ≤2 cm and the highest in size 2–4 cm compared to other groups (P = 0.003).

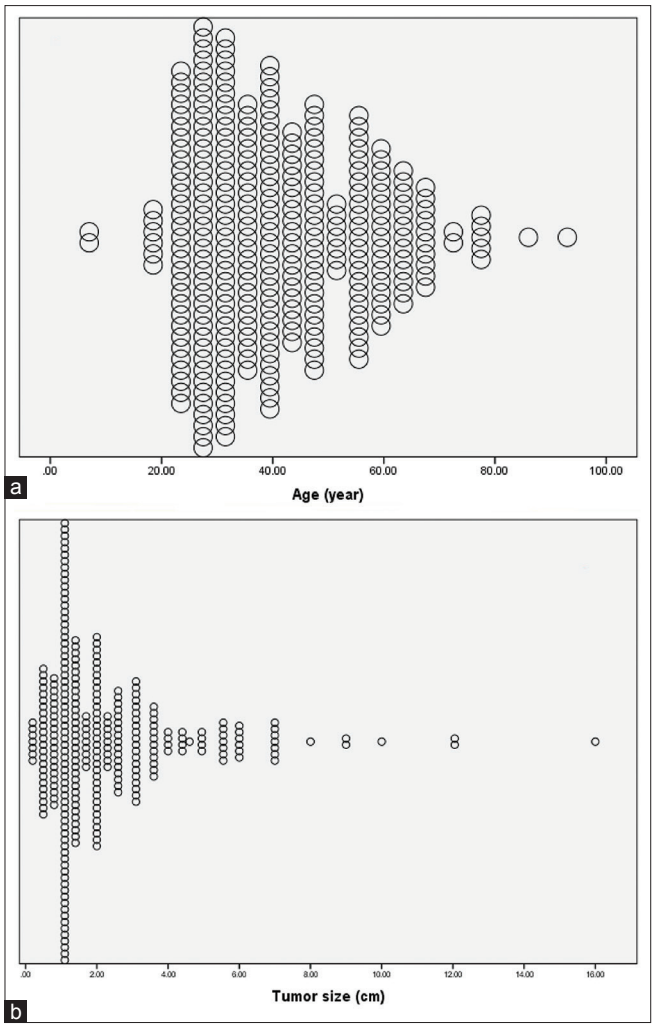

Figure 1: The pattern of distributions of (a) age and (b) tumor size among the patients with thyroid cancer

Discussion

Thyroid nodule is a common endocrine disorder with the frequency being continuously increased worldwide.[14] Thyroid cancer is the fifth most common cancer in women in the U. S.[15] and the third prevalent cancer throughout the world.[4-6] According to reports, thyroid cancer is seen in approximately 1% of all new cancers, and 0.2% of cancer deaths occur in the U. S.[7] Recent studies have shown that

Table 2: Comparison of variables based on sex in the patients with thyroid cancer

Variable	Male (n=74), n (%)	Female (n=222), n (%)	P
Age (year), mean±SD	44.6±16.1	39.9±14.3	0.020
Tumor size (cm), mean±SD	2.0±2.2	2.3±2.0	0.309
Extrathyroidal invasion			
Positive	9 (12.2)	17 (7.7)	0.241
Negative	65 (77.8)	205 (92.3)	
Lymph node metastasis			
Positive	10 (13.5)	53 (23.9)	0.071
Negative	64 (86.5)	169 (76.1)	
Stage			
I	57 (77)	187 (84.2)	0.379
II	9 (12.2)	21 (9.5)	
III	5 (6.8)	11 (5)	
IV	3 (4.1)	3 (1.4)	
Capsular invasion			
Positive	15 (20.3)	46 (20.7)	1.000
Negative	59 (79.7)	176 (79.3)	
Hashimoto's thyroiditis			
Positive	12 (16.2)	68 (30.6)	0.016
Negative	62 (83.8)	154 (69.4)	
Goiter			
Positive	13 (17.6)	37 (16.7)	0.859
Negative	61 (82.4)	185 (83.3)	
Laterality			
Bilateral	6 (8.1)	25 (11.3)	0.636
Right	43 (58.1)	117 (52.7)	
Left	25 (33.8)	80 (36)	
Vascular invasion (n=287)			
Positive	11 (15.3)	37 (17.2)	0.855
Negative	61 (84.7)	178 (82.8)	

SD: Standard deviation

Table 3: Comparison of variables based on the age group in the patients with thyroid cancer

Variable	<45 years (*n*=186), *n* (%)	≥45 years (*n*=110), *n* (%)	*P*
Sex			
Male	37 (19.9)	37 (35.6)	0.012
Female	149 (80.1)	73 (64.6)	
Tumor size (cm), mean±SD	2.1±2.1	2.4±2.1	0.262
Extrathyroidal invasion			
Positive	17 (9.1)	9 (8.2)	0.835
Negative	169 (90.9)	101 (91.8)	
Lymph node metastasis			
Positive	46 (24.7)	17 (15.5)	0.077
Negative	140 (75.3)	93 (84.5)	
Capsular invasion			
Positive	34 (18.3)	27 (24.5)	0.234
Negative	152 (81.7)	83 (75.5)	
Hashimoto's thyroiditis			
Positive	58 (31.2)	22 (20)	0.042
Negative	128 (68.8)	88 (80)	
Goiter			
Positive	25 (13.4)	25 (22.7)	0.053
Negative	161 (86.6)	85 (77.3)	
Laterality			
Bilateral	18 (9.7)	13 (11.8)	0.839
Right	101 (54.3)	59 (53.6)	
Left	67 (36)	38 (34.5)	
Vascular invasion (*n*=287)			
Positive	32 (17.8)	16 (15)	0.625
Negative	148 (82.2)	91 (85)	

SD: Standard deviation

the frequency of thyroid cancer is steadily increasing in the world.[8,16] However, the frequency of thyroid cancer has decreased in few countries such as Norway and Sweden.[17] Thyroid cancer can occur at any age. In the present study, the mean age of patients was 41.1 years, and the highest number of patients belonged to the age range <45 years. The mean age was in consistent with the study conducted in Yazd, Iran. They found the mean age of 41.91 years, but their patients were equally distributed in two age groups of more or <40 years.[18] In the study of Taghavi Kojidi *et al*. in Iran, the prevalence of thyroid cancer was the highest in patients over 70 years.[19] Another study showed the highest number of patients were in the age group younger than 30 years.[20] Some of these discrepancies may be due to different age groups of patients in different studies. Better judgment will be possible if pathological subtypes are taken into account. The female/male ratio of thyroid cancer in this study was 3/1, which was consistent with the previous surveys in Iran and other countries.[21-23] The frequency of PTC has been estimated to increase while the frequency of FTC and MTC has remained relatively stable and that of ATC has declined.[8] Furthermore, the frequency of thyroid cancer is variable among different countries, which is directly linked to decisions made concerning the diagnosis and treatment. Among 296 patients in our study, papillary carcinoma was the most frequent one with a frequency of 89%, followed by follicular, medullary, and anaplastic carcinomas (8%, 1.7%, and 1.4%, respectively). PTC was more frequent in the current study than in other studies in Iran.[21,24-26] However, there are studies in the United States, France, and Japan that have demonstrated a higher prevalence for PTC than our study (>90%).[27-29] About 11% (29 cases) of papillary carcinomas had follicular variant, which was diagnosed histologically.

The high variation in thyroid cancer in geographic areas found in different studies originates from the genetic, environmental, and lifestyle factors. Access to medical care is also a determinant.[14] LNs invasion, extrathyroid invasion, capsular invasion, and vascular invasion have been observed with prevalence rates of 21.3%, 8.8%, 20.6%, and 16.7%, respectively. Lee *et al*. reported higher capsule invasion and extrathyroidal extension than our study.[10] In addition, they showed a statistically significant difference in central LN metastasis (P = 0.005), capsular invasion (P = 0.0001), and extrathyroidal extension (P = 0.005).

LNs metastasis is an important determinant of the prognosis of PTC.[30] Lymphatic invasion is associated with metastasis to nodes in the central or lateral compartments.[31] The present study demonstrated LNs invasion in 21.3% of cases. We did not find any significant difference in LN metastasis between both age groups and genders. Meanwhile, larger tumor size was not statistically associated with a higher risk for LN metastasis. It means that small tumors ≤2 cm have a risk of metastasis, so better evaluation of suspicious thyroid nodules and faster treatment even in small tumors are suggested accordingly. Most patients in both genders were in Stage I. The number of cases decreased with a rise in the Stage from I to IV. This may be due to more sensitive imaging techniques or awareness of the population of significant thyroid nodules and seeking diagnosis and treatment. The fine-needle aspiration is routinely done and educated in this center and is routinely used for diagnosis of suspicious thyroid lesions.

Hashimoto thyroiditis was frequently noted adjacent to thyroid cancers with significant association in young women. Evidently, autoimmune disorders, including Hashimoto thyroiditis in both acute and chronic phases are more frequent among women.[32] We found most tumors on the right thyroid lobe with statistically significant association with tumor size. Dellal *et al*.[33] found more laterality in the right side in both exophytic and nonexophytic nodules but with no evaluation for P value. It seems that a higher number of cases and more definite identification of laterality and multifocality versus

Table 4: Comparison of variables based on tumor size in the patients with thyroid cancer

Variable	≤2 cm (*n*=196), *n* (%)	2-4 cm (*n*=64), *n* (%)	>4 cm (*n*=36), *n* (%)	*P*
Age (year), mean±SD	4.6±1.5	4.4±1.5	4.5±1.4	0.697
Sex				
Male	54 (27.6)	13 (20.3)	7 (19.4)	0.364
Female	142 (72.4)	51 (79.7)	29 (80.6)	
Extrathyroidal invasion				
Positive	22 (11.2)	2 (3.1)	2 (5.6)	0.106
Negative	174 (88.8)	62 (96.9)	34 (94.4)	
Lymph node metastasis				
Positive	46 (23.5)	9 (14.1)	8 (22.2)	0.277
Negative	150 (76.5)	55 (85.9)	28 (77.8)	
Capsular invasion				
Positive	34 (17.3)	17 (26.6)	10 (27.8)	0.150
Negative	162 (82.7)	47 (73.4)	26 (72.2)	
Hashimoto's thyroiditis				
Positive	58 (29.6)	18 (28.1)	4 (11.1)	0.070
Negative	138 (70.4)	46 (71.9)	32 (88.9)	
Goiter				
Positive	37 (18.9)	6 (9.4)	7 (19.4)	0.193
Negative	159 (81.1)	58 (90.6)	29 (80.6)	
Laterality				
Bilateral	15 (7.7)	13 (20.3)	3 (8.3)	0.043
Right	107 (54.6)	30 (46.9)	23 (63.9)	
Left	74 (37.8)	21 (32.8)	10 (27.8)	
Vascular invasion (*n*=287)				
Positive	22 (11.5)	18 (29.5)	8 (22.9)	0.003
Negative	169 (88.5)	43 (70.5)	27 (77.1)	

SD: Standard deviation

unifocality are needed to gain better insight into this matter.

Conclusions

This study reported the data of thyroid cancer in Kermanshah, Iran, for the first time. The mean age and female/male ratio in this study were similar to other areas of Iran. PTC is the most common kind of thyroid cancer in Iran. In addition, the role of Hashimoto's thyroiditis in Iranian patients with thyroid cancer should be taken into consideration in the future. The differences between Iranian studies can be due to different genetic, environmental, and lifestyle factors.

Acknowledgment

The authors would like acknowledge Vice-Chancellor for Research and Technology, Kermanshah University of Medical Sciences and the Clinical Research Development Center of Imam Reza Hospital in Kermanshah.

Financial support and sponsorship

The study was financially supported by the Kermanshah University of Medical Sciences (grant number 96461).

Conflicts of interest

There are no conflicts of interest.

References

1. Kim SH, Park HS, Kim KH, Yoo H, Chae BJ, Bae JS, *et al.* Correlation between obesity and clinicopathological factors in patients with papillary thyroid cancer. Surg Today 2015;45:723-9.
2. Shi X, Liu R, Basolo F, Giannini R, Shen X, Teng D, *et al.* Differential clinicopathological risk and prognosis of major papillary thyroid cancer variants. J Clin Endocrinol Metab 2016;101:264-74.
3. Safavi A, Azizi F, Jafari R, Chaibakhsh S, Safavi AA. Thyroid cancer epidemiology in Iran: A time trend study. Asian Pac J Cancer Prev 2016;17:407-12.
4. Horn-Ross PL, Chang ET, Clarke CA, Keegan TH, Rull RP, Quach T, *et al.* Nativity and papillary thyroid cancer incidence rates among hispanic women in California. Cancer 2012;118:216-22.
5. Bann DV, Goyal N, Camacho F, Goldenberg D. Increasing incidence of thyroid cancer in the commonwealth of Pennsylvania. JAMA Otolaryngol Head Neck Surg 2014;140:1149-56.
6. Ban EJ, Andrabi A, Grodski S, Yeung M, McLean C, Serpell J. Follicular thyroid cancer: Minimally invasive tumours can give rise to metastases. ANZ J Surg 2012;82:136-9.
7. LiVolsi VA. Papillary thyroid carcinoma: An update. Mod Pathol 2011;24 Suppl 2:S1-9.
8. Sipos JA, Mazzaferri EL. Thyroid cancer epidemiology and prognostic variables. Clin Oncol (R Coll Radiol) 2010;22:395-404.
9. Tarui T, Ishikawa N, Kadoya S, Watanabe G. Co-occurrence of papillary thyroid cancer and MALT lymphoma of the thyroid

with severe airway obstruction: A case report and review of the literature. Int J Surg Case Rep 2014;5:594-7.
10. Lee SG, Ho J, Choi JB, Kim TH, Kim MJ, Ban EJ, *et al.* Optimal cut-off values of lymph node ratio predicting recurrence in papillary thyroid cancer. Medicine (Baltimore) 2016;95:e2692.
11. Kang YE, Kim KS, Park SJ, Jung SN, Chang JW, Yi S, *et al.* High expression of angiopoietin-1 is associated with lymph node metastasis and invasiveness of papillary thyroid carcinoma. World J Surg 2017;41:3128-38.
12. Randle RW, Balentine CJ, Leverson GE, Havlena JA, Sippel RS, Schneider DF, *et al.* Trends in the presentation, treatment, and survival of patients with medullary thyroid cancer over the past 30 years. Surgery 2017;161:137-46.
13. Lee JH, Ahn HK, Seok JY, Lee KC, Chun YS, Chung YS, *et al.* Optimal combination of treatment modality to increase survival in patients with anaplastic thyroid carcinoma: A STROBE compliant retrospective study. Medicine (Baltimore) 2018;97:e11037.
14. Pellegriti G, Frasca F, Regalbuto C, Squatrito S, Vigneri R. Worldwide increasing incidence of thyroid cancer: Update on epidemiology and risk factors. J Cancer Epidemiol 2013;2013:965212.
15. Meza R, Chang JT. Multistage carcinogenesis and the incidence of thyroid cancer in the US by sex, race, stage and histology. BMC Public Health 2015;15:789.
16. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. CA Cancer J Clin 2015;65:5-29.
17. Kilfoy BA, Zheng T, Holford TR, Han X, Ward MH, Sjodin A, *et al.* International patterns and trends in thyroid cancer incidence, 1973-2002. Cancer Causes Control 2009;20:525-31.
18. Vahedian Ardakani HA, Moghimi M, Shayestehpour M, Doosti M, Beigi Sharifabadi S. Survival of patients with thyroid cancer in Yazd, Iran Asian Pac J Cancer Prev 2017;18:2293-7.
19. Taghavi Kojidi H, Farzadfar F, Peykari N, Larijani B, Rahimzadeh S, Rezaei-Darzi E, *et al*. A comprehensive study on national and sub national trend in thyroid cancer prevalence in the Iranian population, 1990–2010. Iranian J Diabetes Metab 2016;15:91-100.
20. Khayamzadeh M, Khayamzadeh M, Tadayon N, Salmanian R, Zham H, Razzaghi Z, *et al.* Survival of thyroid cancer and social determinants in Iran, 2001-2005. Asian Pac J Cancer Prev 2011;12:95-8.
21. Haghpanah V, Soliemanpour B, Heshmat R, Mosavi-Jarrahi AR, Tavangar SM, Malekzadeh R, *et al.* Endocrine cancer in iran: Based on cancer registry system. Indian J Cancer 2006;43:80-5.
22. Links TP, van Tol KM, Jager PL, Plukker JT, Piers DA, Boezen HM, *et al.* Life expectancy in differentiated thyroid cancer: A novel approach to survival analysis. Endocr Relat Cancer 2005;12:273-80.
23. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. CA Cancer J Clin 2016;66:7-30.
24. Larijani B, Mohagheghi MA, Bastanhagh MH, Mosavi-Jarrahi AR, Haghpanah V, Tavangar SM, *et al.* Primary thyroid malignancies in Tehran, Iran. Med Princ Pract 2005;14:396-400.
25. Thoresen S, Akslen L, Glattre E, Haldorsen T, Lund E, Schoultz M. Survival and prognostic factors in differentiated thyroid cancer – A multivariate analysis of 1,055 cases. Br J Cancer 1989;59:231.
26. Scheiden R, Keipes M, Bock C, Dippel W, Kieffer N, Capesius C, *et al.* Thyroid cancer in luxembourg: A national population-based data report (1983-1999). BMC Cancer 2006;6:102.
27. Li JY, Shi J, Sang JF, Yao YZ, Wang XC, Su L, *et al.* Role of survivin in the pathogenesis of papillary thyroid carcinoma. Genet Mol Res 2015;14:15102-11.
28. Colonna M, Bossard N, Guizard AV, Remontet L, Grosclaude P; le réseau FRANCIM. Descriptive epidemiology of thyroid cancer in France: incidence, mortality and survival. Ann Endocrinol (Paris) 2010;71:95-101.
29. Tsukuma H, Ajiki W, Ioka A, Oshima A. Research Group of Population-Based Cancer Registries of Japan. Survival of cancer patients diagnosed between 1993 and 1996: A collaborative study of population-based cancer registries in Japan. Jpn J Clin Oncol 2006;36:602-7.
30. Czarniecka A, Jarzab M, Krajewska J, Chmielik E, Szcześniak-Klusek B, Stobiecka E, *et al.* Prognostic value of lymph node metastases of differentiated thyroid cancer (DTC) according to the local advancement and range of surgical excision. Thyroid Res 2010;3:8.
31. Chung YS, Kim JY, Bae JS, Song BJ, Kim JS, Jeon HM, *et al.* Lateral lymph node metastasis in papillary thyroid carcinoma: Results of therapeutic lymph node dissection. Thyroid 2009;19:241-6.
32. Fairweather D, Frisancho-Kiss S, Rose NR. Sex differences in autoimmune disease from a pathological perspective. Am J Pathol 2008;173:600-9.
33. Dellal FD, Baser H, Arpaci D, Tam AA, Ozdemir D, Kilicarslan A, *et al*. Rate of malignancy in exophytic thyroid nodules. Iran J Radiol 2017;14:e41141.