

RESEARCH ARTICLE

Survival of Patients with Thyroid Cancer in Yazd, Iran

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Abstract

Background: Thyroid cancer is the most common endocrine related malignancy in the world. This cancer has increased during recent years in Iran and is the 11th most common malignancy in Iranian population. Survival of patients with thyroid carcinoma in the different geographic areas within Iran is not clear. The present study aimed to estimate survival of patients suffering from thyroid cancer in Yazd, Iran. **Methods:** In this retrospective cohort study, data were collected from 80 patients with thyroid cancer registered in Shohadaye Kargar and Shahid Sadoughy hospitals in Yazd between March 2001 and March 2012. The Kaplan-Meier analysis was used for estimation of survival over time and Cox regression method was performed for calculating hazard ratios according to demographic and risk variables. **Results:** Survival rates at the end of 1, 3, and 5 years in thyroid cancer patients were 99%, 96%, and 91%, respectively. A statistically significant correlation was found between stage of disease, type of cancer and survival time of patients ($p < 0.05$). The worst survival was in peoples with the anaplastic type and stage IV of thyroid carcinoma. **Conclusion:** The survival of patients with thyroid carcinoma was higher than some areas in Iran. Since type and stage of thyroid cancer were the important factors in survival time, screening of people for cancer diagnosis in early stages, it seems to improve survival of patients. Radioactive iodine therapy can increase the survival rate in patients suffering from thyroid malignancy.

Keywords: Survival- Thyroid cancer- Iran

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Introduction

Thyroid cancer is the most common malignancy associated with endocrine system. More than 213,000 new cases of thyroid malignancy occur annually worldwide that it causes approximately 35,000 death each year (Safavi et al., 2016). In most countries, incidence of thyroid cancer is less than five cases per 100,000 population in both men and women (Khayamzadeh et al., 2011). The estimated incidence rate of thyroid carcinoma was 2.20 per 100,000 people per year in Iran (Safavi et al., 2016). During the last decades, thyroid cancer incidence among both sex has raised in many countries, because of the increased detection of malignancy in the early stage (Pellegriti et al., 2013; Kitahara and Sosa, 2016; Pearce, 2017). Thyroid cancer is now the fastest growing malignancy type and the sixth most commonly diagnosed cancer worldwide (Melak et al., 2014). This cancer is 11th most common cancer in both sexes, 14th in male and the 7th most frequent malignancy in female in Iran (Khayamzadeh et al., 2011).

Survival rate of thyroid carcinoma is better than most other cancers (Melak et al., 2014). In USA, the 5 and 10-year survival rates for patients with thyroid malignancy are 98% and 97%, respectively (Howlader et al., 2015).

The type of tumor is the most important prognostic factor for thyroid carcinoma. Papillary thyroid cancer has the best prognosis and response to treatment. Follicular and medullary carcinomas have the good prognosis, but less favorable than papillary carcinoma. Anaplastic thyroid cancer has a very poor prognosis (Sipos and Mazzaferri, 2010). Overall 5-year survivals for patients with papillary, follicular, medullary and anaplastic thyroid cancer are reported 96%, 91%, 80% and 14%, respectively (Biersack and Grünwald, 2005).

Unique among cancers, age is a main prognostic factor for papillary and follicular thyroid carcinomas. Patients under 45 years old have a good prognosis and older people have a less favorable prognosis (Haymart, 2009). The highest rate of thyroid carcinoma is reported in people aged 45 years in Iran (Safavi et al., 2016). The incidence rate of thyroid cancer in females is higher than males, but this cancer generally in men has a worse prognosis than in women. Therefore, in some reports sex is mentioned as a prognostic factor (Khayamzadeh et al., 2011).

Cancer survival statistics can be useful for determining prognosis and evaluating treatment options. Therefore, knowing about cancer survival rates in any country is necessary. Thyroid cancer survival rates are different

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considerably between developing and developed countries in terms of the public health care system; access to diagnosis, treatment facilities and effective treatment protocols (Vecchia et al., 2015). According to available data, the trend of thyroid cancer incidence is increasing in Iran (Safavi et al., 2016), but published data on survival of patients with thyroid cancer are not enough. In 2010, Yazd province had the highest incidence of thyroid carcinoma among all areas in Iran (Taghavi et al., 2016). The present study aimed to determine the survival of patients with thyroid cancer in Yazd, Iran.

Materials and Methods

In this retro perspective cohort study, data were obtained from 80 patient suffering from thyroid cancer registered in Shohadaye Kargar and Shahid Sadoughy hospitals in Yazd between March 2001 and March 2012. The inclusion criterion was patients with thyroid carcinoma confirmed by two pathologists. The exclusion criteria were patients aged under 18 years old and people

with incomplete medical records. Deaths due to other causes were excluded from this study. Data were collected by a questionnaire and referring to patient records. In addition, thyroid cancer patients were followed-up via phone contact for knowing of them current status. In this study, variables included age, gender, stage of cancer and type of treatment. Data were analyzed using SPSS software version 17 (Chicago, IL, USA). Qualitative variables were reported as proportions and continuous variables as mean \pm SEM. Kaplan-Meier analysis was performed to estimate survival in patients with thyroid cancer and differences in survival time were analyzed by log-rank test. A Multivariate analysis was tried out using the Cox proportional hazard model. In all tests, a p-value less than 0.05 was considered as significant.

Results

In the present study, 80 patients with thyroid carcinoma were followed up. Finally, 73 cases (91.25%) were alive and seven patients (8.75%) died due to thyroid malignancy.

Table 1. Survival Rates in Patients with Thyroid Cancer According to Variables.

Variable	Number (%)	Survival rate (%)			Mean survival time \pm SE (month)	P value
		1 year	3 year	5 year		
Gender						
Male	27 (33.75)	100	93	82	116.61 \pm 3.88	0.161
Female	53 (66.25)	98	98	95	130.68 \pm 6.46	
Total	80 (100)	99	96	91	127.01 \pm 4.32	
Age (year)						
19-39	40 (50)	100	100	97	3.21 \pm 135.7	0.0568
40-79	40 (50)	98	92	85	118.8 \pm 7.52	
Type of thyroid cancer						
Papillary	61 (76.25)	100	100	93	132.51 \pm 3.62	<0.05
Follicular	8 (10)	100	100	100	105.33 \pm 10.34	
Anaplastic	1 (1.25)	100	0	0	16	
Medullary	10 (12.50)	90	80	80	114.1 \pm 15.85	
Stage						
I	33 (42.25)	100	100	100	-	<0.05
II	15 (18.75)	100	100	100	-	
III	9 (11.25)	100	100	100	-	
IV	9 (11.25)	90	67	30	44.85 \pm 1.98	
Unknown	14 (17.50)	100	100	100	-	
Treatment						
subtotal Thyroidectomy	74 (92.50)	100	100	100	-	0.435
total Thyroidectomy	6 (7.50)	99	96	90	126.02 \pm 4.66	
Radioiodine Therapy	yes 62 (77.50)	100	100	95	131.9 \pm 3.59	0.013
	No	95	83	77	111.47 \pm 12.31	
chemotherapy	Yes 1 (1.25)	75	50	-	31.75 \pm 11.76	<0.05
	No	100	98	95	131.67 \pm 3.95	
levothyroxine therapy	Yes 4 (5)	99	96	91	126.77 \pm 4.14	0.708
	No	100	100	100	-	
Radiotherapy	Yes 79 (98.75)	100	0	0	16	<0.05
	No	100	98	90	128.46 \pm 4.13	

Distribution of patients with thyroid cancer according to different variables is shown in Table 1. The mean age of total patients was 41.91 years (range, 19-80 yr.). The mean survival time of patients with thyroid cancer was 127.01±4.32 month. Women had the higher mean survival time than men, but this difference was not statistically significant (P=0.161, Table 1). Five-year thyroid cancer survival rate was estimated 91% for all patients and was obtained 82% for men and 90% for women. Patients in age group 19-39 had the better survival rate than that age group 40-79, but survival was not significantly different between the two age groups (p=0.0568, Table 1). In this study, the cancer survival time was estimated for patients in different types and stages of thyroid carcinoma. Patients with papillary thyroid cancer had the largest survival time (132.51±3.62 month) while people with anaplastic thyroid carcinoma had the lowest mean survival time (16 month). The worst survival was seen in patients with stage IV thyroid cancer that had a 5-year survival time equal to 30% (Table 1). Seventy four cases were treated with total thyroidectomy that had not been a significantly lower survival period than those treated by Subtotal Thyroidectomy (P=0.435). Data obtained from comparing patients treated and untreated with radioiodine showed that radioactive iodine treatment is increased significantly survival time in thyroid cancer patients (P=0.013). Results of the multivariate survival analysis using Cox regression method are summarized in Table 2.

Table 2. Results of Multivariate Survival Analysis Using Cox Regression Method

Variable	Hazard Ratio	Confidence Interval (95%)	P value
Gender			
Male	1	-	Ref
Female	0.382	0.086-1.707	0.208
Age (year)			
19-39	1	-	Ref
40-79	6	0.597-43.761	0.097
Type of thyroid cancer			
Papillary	1	-	Ref
Follicular	2.5	0.26-24.034	0.427
Anaplastic	20	2.080-192.271	0.009
Medullary	4	0.668-23.939	0.129
Stage			
I	1	-	Ref
II	1	-	1
III	1	-	1
IV	53657	0-4.97	0.812
Unknown	1	-	1
Treatment			
total	1	-	Ref
Thyroidectomy			
subtotal	0.044	0-10902	0.623
Thyroidectomy			
Radioiodine Therapy	No	1	Ref
	Yes	0.218	0.049-0.973

Data revealed that patients in age range of 40-79-year-old had the risk of thyroid cancer six times more compared with those between 19 and 39 years old. Anaplastic thyroid carcinoma was associated with 20 times increased risk of death in patients compared with other types of thyroid cancers. Radioiodine therapy significantly decreased HR for thyroid carcinoma mortality risk (HR: 0.218).

Discussion

This study was designed to estimate the survival of patients with thyroid carcinoma in Yazd province of Iran. The gender distribution of patients in this study was lower than other studies, approximately two times higher in females compared with males. In an epidemiologic study in Iran, the female to the male ratio was 3/1 (Larijani et al., 2005), similar to another reports in Luxemburg, Norway and Netherlands (Eustatia-Rutten et al., 2006).

In this study, the mean age at the time of diagnosis was 41.91 years, and an equal number of cases were in two age groups under 40 and upper 40 years old. In Iran, the thyroid cancer incidence was the highest in patients upper 70 years old from 1990 to 2010 (Taghavi et al., 2016). In a study conducted in Tehran, the age distribution of thyroid carcinoma had two peaks of incidence in age group 45-60 and upper 65 years old (Larijani et al., 2005). In another study in Iran, the mean age of patients with thyroid cancer was 44.5 years old, and the highest number of people were in the age group younger than 30 years old (Khayamzadeh et al., 2011). Because of different age classification in each study, the results are not comparable. A cause of this variation may be the unlike population size in each age group in the different area. However, in the current study, incidence of thyroid cancer in Yazd between 2001 and 2012 in the age group 19-39 years was similar to 40-79 years.

In the present study, the data analysis indicated that the overall survival rate for all patients with thyroid cancer at the end of one, three and five years were 99%, 96%, and 91%, respectively (Table1). Therefore, thyroid cancer patients had a high long-term survival rate. In French, One-year and five-year overall survivals were reported 94% and 93%, respectively (Colonna et al., 2010). In study of Tsukuma in Japan, the five-year survival rate for patients with thyroid cancer was 87% (Tsukuma et al., 2006). According to the published data, the 5-year survival outcome for patients suffered from thyroid carcinoma was 82% in Thailand (Sankaranarayanan et al., 1998), 92% in Luxemburg (Scheiden et al., 2006) and 98% in USA (Blackburn et al., 2017). Therefore, thyroid carcinoma survival times can be varied widely between countries due to different in socioeconomic status, screening, and the early diagnosis of the disease using new facilities.

The reported survival rates in areas with unlike socio-economic status in Iran were different. The five-year survival rate has been varied from 77% in Azerbaijan (Northwest Iran) to 97% in Khuzestan province, located southwestern of Iran. It is 89% in Tehran and 95% in Esfahan as central part of Iran. Our result showed that the 5-year survival outcome in Yazd city located in the eastern

part of central Iran was 91%. People living in Yazd city have a high socio-economic condition; therefore, they have a higher cancer survival rate than those living in Azerbaijan, Kermanshah, Kerman and Khorasan. The obtained survival rate of the population with thyroid carcinoma in Yazd was lower than the survival rate reported from Mazandaran (Khayamzadeh et al., 2011). In two studies conducted in Iran, the five-year survival rate for patients with thyroid carcinoma was reported 82% and 88% (Larijani et al., 2005; Khayamzadeh et al., 2011), that are lower than our finding, because the number of cases in those reports were more than our study, and most patients had high stage disease.

The five-year survival rate in Yazdian males and females with thyroid cancer was 82% and 95%, respectively, but no significant difference was seen between survivals of the two sexes ($p=0.161$). Larijani et al., (2005) have obtained similar finding in their study. However, Khayamzadeh et al., (2011) were reported the survival rate of thyroid cancer in women significantly higher than man. In addition to, we have not observed a statistically significant correlation in the survival rate between the age groups lower 40 and upper 40 years old. This data is in contrast with those studies that were reported a significant decreased survival in people over 40 years old (Haymart, 2009; Miyauchi, 2016). The possible cause of this difference is the lower frequency of undifferentiated tumors in our study, which happen after age 40 years and cause a low survival rate.

Based on multivariate survival analysis in this study, types of thyroid cancer and stage of disease were as effective factors in prognosis. Patients with anaplastic thyroid carcinoma or stage IV of cancer were in higher risk of death compared with other types and stages of thyroid cancer. These findings were comparable with other reports. Many studies were shown that mortality in patient suffered from thyroid cancer stage IV, and anaplastic form was high (Khayamzadeh et al., 2011; Fardmal et al., 2016). In the current study, treatment with radioiodine was significantly increased the survival rate in thyroid cancer patients. This data is consistent with some studies that believe to improve the survival rate of patients after use of radioactive iodine (Ruel et al., 2015; Clerc et al., 2017). However, some researchers cannot approve a survival benefit of radioactive iodine therapy (Schvartz et al., 2012).

This study has several limitations, such as incomplete medical records, failure to refer patients for follow up and poor corporation of some patients during phone contact. Therefore, some peoples exclude from study and the number of participants decreased. However, an adequate sample size was chosen based on statistical calculation.

In conclusion, the survival rate of patients with thyroid carcinoma in this study was higher than some areas in Iran. Since type and stage of thyroid cancer were the important factors in survival time, screening of people for cancer diagnosis in early stages, it seems to improve survival of patients. Radioactive iodine therapy can increase the survival rate in patients suffering from thyroid malignancy.

References

- Biersack HJ, Grünwald F (2005). *Thyroid cancer*, Springer Berlin Heidelberg.
- Clerc J, Verburg FA, Avram AM, et al (2017). Radioiodine treatment after surgery for differentiated thyroid cancer: a reasonable option. *Eur J Nucl Med Mol Imaging*, **44**, 918-25.
- Colonna M, Bossard N, Guizard AV, et al (2010). Descriptive epidemiology of thyroid cancer in France: incidence, mortality and survival. *Ann Endocrinol (Paris)*, **71**, 95-101.
- Eustatia-Rutten CF, Corssmit EP, Biermasz NR, et al (2006). Survival and death causes in differentiated thyroid carcinoma. *J Clin Endocrinol Metab*, **91**, 313-9.
- Fardmal J, Ghafari ME, Zakavi SR, et al (2016). Predicting of disease free survival in patients with thyroid cancer and its influencing factors during 1978 to 2012. *J Shahrekord Univ Med Sci*, **18**, 78-86.
- Haymart MR (2009). Understanding the relationship between age and thyroid cancer. *Oncologist*, **14**, 216-21.
- Khayamzadeh M, Khayamzadeh M, Tadayon N, et al (2011). Survival of thyroid cancer and social determinants in Iran, 2001-2005. *Asian Pac J Cancer Prev*, **12**, 95-8.
- Kitahara CM, Sosa JA (2016). The changing incidence of thyroid cancer. *Nat Rev Endocrinol*, **12**, 646-53.
- Larijani B, Mohagheghi MA, Bastanagh MH, et al (2005). Primary thyroid malignancies in Tehran, Iran. *Med Princ Pract*, **14**, 396-400.
- Melak T, Mathewos B, Enawgaw B, et al (2014). Prevalence and types of thyroid malignancies among thyroid enlarged patients in Gondar, Northwest Ethiopia: a three years institution based retrospective study. *BMC Cancer*, **14**, 899.
- Miyauchi A (2016). Clinical trials of active surveillance of papillary microcarcinoma of the Thyroid. *World J Surg*, **40**, 516-22.
- Pearce EN (2017). Thyroid cancer overdiagnosis is a result of screening programs in South Korea. *Clin Thyroidol*, **29**, 8-10.
- Pellegriti G, Frasca F, Regalbuto C, et al (2013). Worldwide increasing incidence of thyroid cancer: update on epidemiology and risk factors. *J Cancer Epidemiol*, **2013**, 965212.
- Ruel E, Thomas S, Dinan M, et al (2015). Adjuvant radioactive iodine therapy is associated with improved survival for patients with intermediate-risk papillary thyroid cancer. *J Clin Endocrinol Metab*, **100**, 1529-36.
- Safavi A, Azizi F, Jafari R, et al (2016). Thyroid cancer epidemiology in Iran: a time trend study. *Asian Pac J Cancer Prev*, **17**, 407, 12.
- Sankaranarayanan R, Black RJ, Swaminathan R, et al (1998). An overview of cancer survival in developing countries. *IARC Sci Publ*, **145**, 135-73.
- Scheiden R, Keipes M, Bock C, et al (2006). Thyroid cancer in Luxembourg: a national population-based data report (1983-1999). *BMC Cancer*, **6**, 102.
- Schvartz C, Bonnetain F, Dabakuyo S, et al (2012). Impact on overall survival of radioactive iodine in low-risk differentiated thyroid cancer patients. *J Clin Endocrinol Metab*, **97**, 1526-35.
- Sipos J, Mazzaferri E (2010). Thyroid cancer epidemiology and prognostic variables. *Clin Oncol*, **22**, 395-404.
- Taghavi KH, Farzadfar F, Peykari N, et al (2016). A comprehensive study on national and sub national trend in thyroid cancer prevalence in the iranian population, 1990–2010. *J Diabetes Metab Disord*, **15**, 91-100.
- Tsukuma H, Ajiki W, Ioka A, et al (2006). Survival of cancer patients diagnosed between 1993 and 1996: a collaborative study of population-based cancer registries in Japan.

Jpn J Clin Oncol, **36**, 602-7.
Vecchia C, Malvezzi M, Bosetti C, et al (2015). Thyroid cancer mortality and incidence: a global overview. *Int J Cancer*, **136**, 2187-95.