RESEARCH COMMUNICATION

Survival of Thyroid Cancer and Social Determinants in Iran, 2001-2005

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Abstract

Background: Thyroid cancer is the most common endocrine system malignancy in the world, being the 7th most common cancer in females, 14th in males and 11th in both sexes in the Iranian population. The present study aimed to determine survival of thyroid cancers in Iran based on sex, age group, pathology and geographical location. Methods: The patients selected for this study were 602 out of 5,759 cases listed in the cancer registry system between 2001 and 2005. The Kaplan-Meier method was used for survival estimation and Cox's proportional hazard model for calculating hazard ratios according to demographic and risk variables. Results: The overall 5-year survival rate was 88.0%. There was a significant difference between survivals of the two sexes. The best and worst survival were in the age groups under 40 and over 60 years old, respectively. The best survival was for papillary type, with the anaplastic type demonstrating the worst survival. The best survival was in the southwest (Khuzestan) and the worst in the northwest (Azarbaijan). Conclusion: Size of young population and social determinants may be important effective elements for differences in survival, which should be taken more into consideration in managing chronic disease such as thyroid cancer.

Keywords: Thyroid neoplasms - survival rate - Iran

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Introduction

Thyroid cancer is the most common malignancy of endocrine system in the world (Lowenstein et al., 2008; Haghpanah et al., 2006). In most areas, incidence of thyroid cancer among female and male are about 2-5 and 1-2 per 100,000 population respectively, and the incidence rate have been stable or slowly increasing (less than 1%/ year) during the last decades. Mortality rates have steadily decreased, because the detection, care and treatments have been improved (Boyle and Levin, 2008). Thyroid cancer is the 7th most common cancer in females, 14th in the males and the 11th most frequent cancer in both sexes in Iranian population (Akbari et al., 2008). Age standardized rates (ASR) are 4.46 and 1.67 per 100000 for women and men (CDC, 2007-2008). In United States it is consist of less than 1% of all malignancies (2% in females and 0.5 for men) (Brunicardi et al., 2010).

Survival from thyroid cancer is generally very good (more than 85%, five year survival in Europe and North America) with low mortality (less than 1.5/100,000 in women and 0.6/100,000 in men in most areas) (Boyle and Levin, 2008). It has a wide variation in survival rate depending on the histologic type of the tumors. Differentiated tumors such as papillary and follicular type are often curable with good prognosis (Thoresen et al., 1989). Anaplastic thyroid cancer is aggressive with poor prognosis (Liu et al., 2006; Chiacchio et al., 2008; Lowenstein et al., 2008; Neff et al., 2008). The natural status of disease is relatively mild and treatment of the tumor is highly successful.

The most important prognostic factors in thyroid cancer are age (Thoresen et al., 1989; Akslen et al., 1991; Esik et al., 1996; Teppo and Hakulinen, 1998; Gulcelik et al., 2007) and stage (Akslen et al., 1991; Esik et al., 1996; Teppo and Hakulinen, 1998; Lowenstein et al., 2008). In some references factors such as sex, radiation history in childhood, lymphatic involvement and TSH depression are mentioned as prognostic factors.

The incidence of thyroid cancer increases with age, plateauing after age 50 (Lowenstein et al., 2005). Thyroid cancer is twice common in female as male. The estimation of 5-year survival which was done in a study in Tehran (Larijani et al., 2006) was 82.2%, but there is not national data about it. Thus the aim of this study is estimation of thyroid cancers survival rate based on the data of cancer registry system in Iran between 2001 and 2005and distribution of pathology type throughout the country as a evidence base national research about thyroid malignancy and it's management.

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Materials and Methods

The data of cancer registry system which were collected by Ministry of Health & Medical Education (MOHME) based on pathology laboratories reports was the main source for this research. It is estimated that these data cover 80% of cancer cases in the newest year, because hospital based and death certificates were not assumed. Totally 5759 case of thyroid cancer were registered between 2001-2005. Demographic characteristic of the patients such as sex, age group and pathological type were analyzed and reported as a descriptive study. Then, 602 cases were selected from the different clusters all over the country randomly as the sample based on the population size and socioeconomic status and geographical variation with different ethnicity criteria definite in nine separated area by Ministry of health and medical education (MOHME). In order to obtain consistency between total registered patients and the selected cases, which were followed up by calling with a trained nurse, comparison of demographic characteristic such as sex, age group and pathologic type of the thyroid cancer was done. The age was divided into 5 groups and the pathological type which was registered in 55 forms, was classified in 6 groups. The survival duration of cases was determined as the time difference between date of diagnosis and date of follow up or death reported by telephone calling.

The data were analyzed by SPSS software, version 17. The probability curves for survival are constructed according to the Kaplan-Meire method for overall cohort and differences in standardized survival time were tested by log-rank test. Multivariate analysis was carried out the Cox proportional hazard model. In all tests, a two-sided p-value <0.05 was considered to be significant and 95% confidence interval (CI) was given when appropriate.

Results

The total number of 5,759 patients with thyroid cancer was registered between 2001 and 2005 by MOHME and the number of cases which were selected for this study was 602. According to Table 1, we compare the demographic characteristic of the total recorded cases and the selected patients. There was no significant difference between two mentioned groups for sex and age distribution and the pathological types. From the 602 patients which were followed up, 57 cases had died due to thyroid cancer and 545 cases were alive. Of all, 4,149 cases (72%) were women and 1,610 cases (28%) were men. The mean age of total patients at the time of diagnosis were 44.6+/- 16.9(We exclude the patients with the age under the 15 years old from the study). Mean age for women and men were 43.3 +/- 16.3 and 48.1+/- 17.8 (p-value <0.001). One, two, three, four and five year survival calculated by Kaplan-Meier methods were 95%, 92%, 91%, 90% and 88% . The mean survival time was 43.4 months (CI= 41.49-45.34 months). In univariate analysis, comparing men and women, there was significant difference between the survival of two sexes (p-value=0.008). One and five year survival rates were 92% and 83% for men and 97% and 91% for women. The age was divided in 5 groups (<30, 30-39, 40-49, 50-59, >60). The highest number of patients were in the age group which were under 30 years old. The best survival was seen in groups under 40 years old and the worst group for survival rate was group over 60 years old (Figure 1). As we classified the pathologic type into 6 groups, the overall five years survival were as follow: papillary 92%, follicular 89%, modularly 59%, mixed (papillary and follicular type) 96.5%, others (lymphoma, sarcoma, giant cell carcinoma and squamous cell carcinoma) was omitted in the analysis because of low number in the selected cases. The last case with anaplastic carcinoma, lived 31 months. The best survival also the highest numbers of patients were in papillary type, and anaplastic type belongs to worst survival. The groups which was named "others" consist of lymphoma (44), sarcoma (5), giant cell carcinoma (3) and squamous cell carcinoma (5). We divided whole of the country into 9 area as was suggested by MOHME based on geographic pattern and socioeconomic status. Regarding the best survival was in southwest (Khuzestan) area, the worse was estimated in northwest (Azarbaijan).

There were significant difference between the survival of southwest with northwest (p- v=0.006) and northeast (p -v=0.04), northwest and center (p -v=0.01), northeast and center (p -v=0.04) (Table 2). The multivariate analysis for gender, age group and pathological type were performed (Table 3). In the multivariate analysis sex was not as a prognostic factor. The following parameters were associated with a significantly increased HR for thyroid cancer related death mortality risk by multivariate analysis: Age group 50-59 (HR=4.48), Age group 60-69 (HR=8.24) and medullary type (HR=3.58), anaplastic

Table1. Basic Characteristics of Registered Patients and Selected Cases of Thyroid Cancer

	Study population N(%)	Target population N(%)	P value
Gender			
Female	426 (70.8%)	4,149 (72%)	
Male	176 (29.2%)	1,610 (28%)	
Total	602 (100%)	5,759 (100%)	0.5
Age groups			
<30	149 (24.8%)	1,397 (24.3%)	
30-39	109 (18.1%)	1,040 (18.1%)	
40-49	127 (21.1%)	1,099 (19.1%)	
50-59	92 (15.3%)	815 (14.2%)	
>60	117 (19.4%)	1,205 (20.9%)	
Missing	8 (1.3%)	203 (3.5%)	
Total	602 (100%)	5,759 (100%)	0.7
Pathologic type			
Papillary	453 (75.2%)	4,222 (73.3%)	
Follicular	42 (7%)	486 (8.4%)	
Medulary	31 (5.1%)	368 (6.4%)	
Anaplastic	17 (2.8%)	154 (2.7%)	
Mixed	57 (9.5%)	439 (7.6%)	
Others	2 (0.3%)	90 (1.6%)	
Total	602 (100%)	5,759 (100%)	0.8
Death status*			
Survived**	545 (90.6%)	-	
Dead	57 (9.4%)	-	
Total	602 (100%)	-	

*Death status were not available for most cases; **In spite of missing data on age, these cases were kept for survival analysis

Table 2. Survival Rate of Thyroid Cancer by Place of Residence

Region (Place of residence)	One year (%)	Two year (%)	Three year (%)	Four year (%)	Five year (%)
South west (Khuzestan)	99	98	97	97	97
North (Mazandaran)	97	94	94	94	94
Center of North (Tehran)	97	92	89	89	89
Center (Esfahan)	97	96	96	95	95
South (Fars)	95	92	92	92	92
South east (Kerman)	95	86	86	86	86
North east (Khorasan)	94	90	82	82	82
Middle west (Kermanshah)	91	87	87	87	87
Northwest (Azarbaijan)	85	82	77	77	77

Table 3. Hazard Ratios (HR) (95% CI) Estimated by Multivariate Analysis

Gender	
Female	1
Male	1.62 (0.92-2.76)
Age group	
<30	1
30-39	0.68 (0.12-3.76)
40-49	2.27 (0.68-7.58)
50-59	4.48 (1.42-141)
>60	8.24 (2.79-24.3)
Pathological type	1
Follicular	0.88 (0.30-2.52)
Modularly	3.58 (1.63-7.86)
Analaic	14.29 (6.50-31.4)
Mixed	0.51 (0.12-2.16)

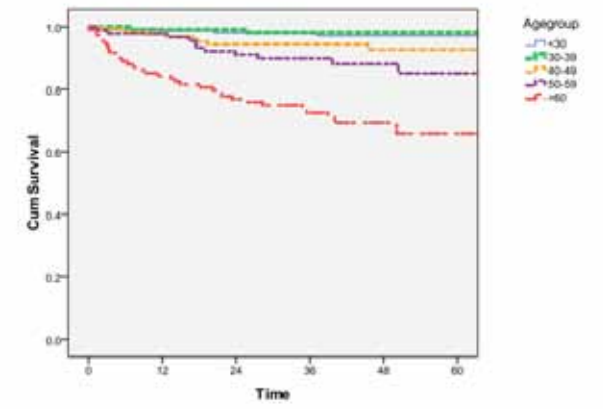

Figure 1. The Kaplan-Mayer Overall Survival Curve of Thyroid Cancer by Age Group

type (HR=14.29).

Discussion

This study evaluates the demographic features and five year survival of thyroid cancer cases from different parts of Iran with different socioeconomic and even ethnicity status as a Middle East country.

The female to male ratio was 2.5/1 which was lower than other studies. In an epidemiologic study in Iran the ratio was reported 3/1(Larijani et al., 2008), similar to another studies in Netherlands (Eustatia-Rutten et al., 2005; Links et al., 2005) and Norway (Akslen et al., 1991) and Luxemburg (Scheiden et al., 2006).

The mean age at diagnosis was 44.5 totally, 43.2 in females and 48 in males and the highest number of patients were in the age group under 30 years old. In another study in Iran, the mean ages were 43.9, 42.5 and 43.4 years old, respectively. In Netherlands it was reported as 47.6 totally and the highest number was in less than 45 years old (Links et al., 2005). In Norway it was in the 55-74 age groups (Thoresen et al., 1989). In Luxemburg (Scheiden et al., 2006) mean age was 48.3 years and the highest numbers (50%) of cases were in the 45-69 age groups. Because of different classifications in studies these are not comparable, but it can be concluded that this cancer is a disease of the younger age group in our country. The main cause of this discrepancy may be the size of population in each age group, for example in Iran, proportion of population under 30 years old is 63% (www.sci.ir2010.) whereas in Norway and Luxemburg are 36% and 37% (www.census.gov/2010).

The distribution of pathological types of TC were 73.3%, 8.4%, 6.4%, 2.7% for papillary, follicular, medullary and anaplastic carcinoma, which were different from other studies. Especially the papillary type were more than in other studies (Thoresen et al., 1989; Hundahl et al., 1998; Haghpanah et al., 2006 ; Scheiden et al., 2006) even comparing to another study in Iran (Larijani et al., 2006) that it was 70%.

The five years survival in our study was 88%, similar to France (Colonna et al., 2010) and Japan (Tsukuma et al., 2006). But it was 82% in Thailand (Sankaranarayanan et al., 1998) and one other study in Iran (Larijani et al., 2006), 94.6% in USA (www.seer.cancer.gov2010) and 92.0% in Luxemburg (Scheiden et al., 2006).

On the basis of univariate analysis of survival, sex, age group and pathologic type were as prognostic. But in multivariate the effect of sex was omitted and was not(Thoresen et al., 1989; Akslen et al., 1991; Eustatia-Rutten et al., 2005; Carmen et al., 2006; Larijani et al., 2005) as a prognostic factor. Age (Thoresen et al., 1989; Akslen et al., 1991; Esik et al., 1996; Hundahl et al., 1998; Eustatia-Rutten et al., 2005; Carmen et al., 2006; Colonna et al., 2010) and pathologic groups (Thoresen et al., 1989; Akslen et al., 1991; Colonna et al., 2010) such as anaplastic type were as known effective factors in prognosis. These results were comparable with other studies. The prognostic factors may change from one population to another and we should be causion in applying on set.

Cares of the patients are similar to each other, but the size of young population, social determinant such as socioeconomic status, geographical variation and the ethnicity are important factors in survival differences. These determinants should be considered in managing chronic disease including malignancies particularly in thyroid cancer. Social determine are effective in survival rate of thyroid cancer and are important subjects for future investigation.

The important issue is the different survival rate in different area of Iran with different socioeconomic and ethnicity variation. The 5 year survival rate differ from 96.5% in upper part of west south (Khuzestan) and 76.5 % in northwest (Azerbaijan) (p-value=0.006) . The main amounts of population in west south (Khuzestan) are Lore and Arab meanwhile in northwest (Azarbaijan) are

Turk. The size of population over 30 years old in these states are 67% and 53% which statistically are significant (p-value<0.05).

By looking at the data, following limitations may be considered. In this study 602 cases out of total 5759 registered patients were analyzed. Because there was no statistical significant difference between these two groups in gender, age group and pathology type distribution, it could be considered as a representative sample of total registered cases in the country. On the other hand, because in Iran, cancer registry system was based on pathology reports, inter-observation variation by different pathologist might be affected the results. Because the data which was used in this study was not complete, we could not evaluate some important factors such as stage and tumor size. These limitations can conducted everyone for further studies.

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