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Impact of Positive Family History on the Survival of Breast Cancer in Iran

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Abstract: To evaluate the influence of family history on the survival of breast cancer in Iranian women, the following study was designed. During 10 years from 1997-2007, 663 women with invasive breast cancer were selected from a private oncology clinic in Isfahan, prospectively. Both demographic variables and tumor characteristics was collected. Analysis was conducted by Cox regression model. A positive family history was found in 125 (19%) patients. Survival rate did not vary between subjects with positive and negative family history of breast cancer in both disease free and overall survival. Cox regression analysis after adjustment for other prognostic factors was determined that family history did not impact on the mortality rate of breast cancer. But lymph node involvement increased the relapse of tumor twice, approximately (RR = 1.9 95% CI = 1.35-2.77). Present findings did not demonstrate any association between breast cancer family history and the prognosis of cancer in Iranian women. It is important that is perceived the family history is a major risk factor for breast cancer but it does not effect on the survival and mortality rate of breast cancer.

Key words: Breast cancer, survival, family history, prognostic factor, risk factor, Iran

INTRODUCTION

Breast cancer is the most frequent cancer in women, this is the commonest cancer in Iranian women, too (Harirchi *et al.*, 2000; Harirchi *et al.*, 2004; Sadjadi *et al.*, 2005). There were several risk and prognostic factors for breast cancer. One of the most important risk factors for breast cancer is the occurrence of breast or ovarian cancer among family members. Women with one or more first-degree relatives with breast cancer have a 1.8-3.0-fold increased risk of developing the disease (Collaborative Group on Hormonal Factors in Breast Cancer, 2001; Pharoah *et al.*, 1997). The prevalence of women with a family history of breast cancer has been estimated to range from 5 to 19% (Murff *et al.*, 2005). After the diagnosis of invasive breast cancer, patients with positive family history are not treated differently compared to patients without a family history. In addition, it has been shown that a strong family history of breast cancer was not associated with a decreased survival after early-onset breast cancer (Verkooijen *et al.*, 2006). There is no study about family history and survival of breast cancer in Iran. The aim of our study was to show any differences in prognostic factors and survival rate between women with a positive family history and negative ones.

MATERIALS AND METHODS

We collected the data from the private oncology clinic in Isfahan. It was only private clinic in Isfahan during 1997 to 2007. Isfahan is a province in central of Iran. The information which was

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collected prospectively during ten years aforementioned period, included demographic/reproductive variables and tumor characteristics by a data collection form. The demographic data contained age, age of menarche, age of marriage, age of first pregnancy, number of child birth, duration of lactation, age of menopause, hormone replacement therapy and family history of breast cancer. Tumor characteristics were tumor size, immuno-histo chemistry (for Estrogen, Progesteron receptors, P53 and c-erb 2 antigene detection), lymph node involvement and grade of tumor. Family history positive was defined that history of breast cancer in the parents, or sisters, or sibling in the breast cancer patients. Survival was calculated by two ways 1- disease free survival was calculated from the date of complete remission as time of surgery to the date of relapse in the patients who achieved complete remission 2-Overall survival from the date of diagnosis to the date of death from breast cancer.

The data were tabulated and analyzed. Kaplan-Meier calculated breast cancer survival rates for women in family history groups and compared with log rank test. Cox regression analysis was conducted to determine hazard rate of family history with controlling of the other prognostic factors. p value <0.05 was considered statistically significant.

RESULTS

In the 10 years period, between 1997 to 2007, 663 women were diagnosed with invasive breast cancer in Isfahan. The mean age of patients was 47.4±10.8. The minimum was 17 and maximum was 79 years old. All patients treated by different chemotherapeutic regimen. A total of 125 (19%) patients reported a positive family history. In Table 1, we present the patients' and tumor characteristics. Most of patients was over 45 years old and were married and had been pregnant at least one time. Tumor size was greater than 2 cm in 83% of women. Overall 61.2% of cases were lymph node positive and had at least 1 to 4 involved lymph node. Kaplan-Meier analysis with log rank test did not determined any significant difference in both disease free and overall survival between two groups of positive and negative family history (Table 2). Overall survival was 95.4 months in patients with positive family history and 94.5 in negative once.

Table 1: Patients ad tumor characteristics

Variables	Frequency	Percent
Age (mean±SD)	47.3±10.8	--
Age of menark (mean±SD)	13.5±5.5	--
Age of 1st pregnancy (mean±SD)	19.8±5	--
Number of pregnancy (mean±SD)	4±2	--
Family history	125	21.0
Tumor size		
<2 cm	93	15.0
2-5 cm	408	63.3
>5 cm	123	19.7
Lymph node involvement		
0	238	38.8
1-4	176	28.7
>4	199	32.5
Estrogen receptor	318	57.0
Progesteron receptor	323	58.0
C- erb 2 receptor	181	59.0
P53	140	32.5
Chemotherapy session		
<8	298	55.3
≥8	241	44.7

Table 2: The mean of survival in family history positive and negative

		Mean±SE	CI 95%	Log rank test p-value
Disease free survival	FHx +	78±4	71-85	0.5018
	FHx -	80±2	76-83	
Overall survival	FHx +	95.4±1.5	92.5-98.3	0.7855
	FHx -	94.5±1.03	92.4-96.5	

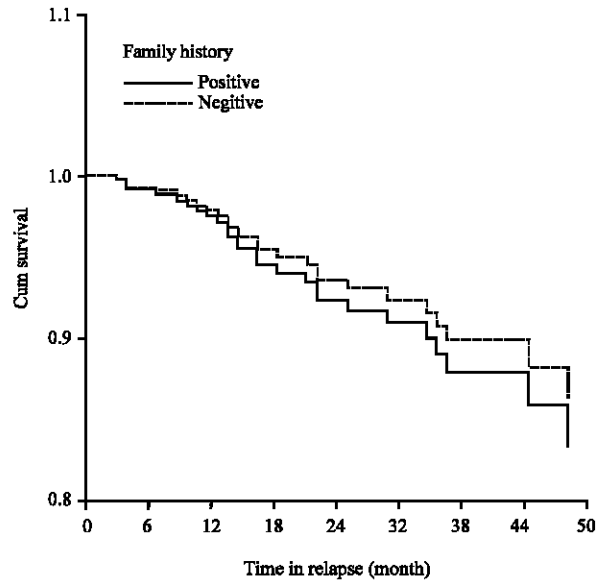


Fig. 1: Disease free survival plot in two positive and negative family history

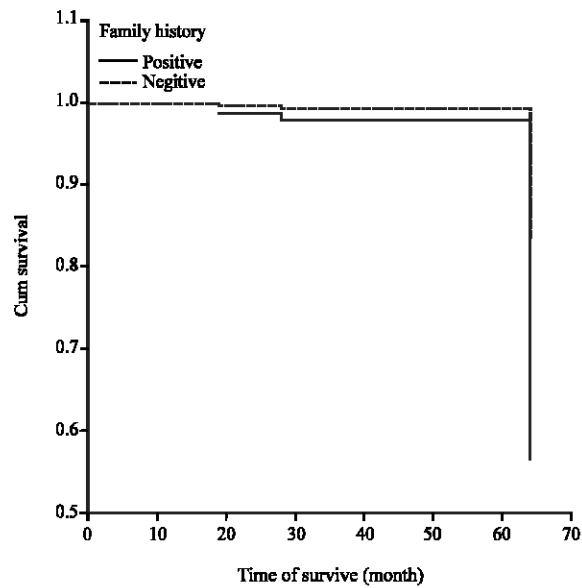


Fig. 2: Overall survival plot in two positive and negative family history

After adjustment for all risk factors, there was not significantly difference among survival of women at positive familial risk compared to those at negative familial risk in disease free and overall survival (Fig. 1 and 2).

Table 3 and 4 presents the breast cancer mortality risks of patients with a positive family history compared to those at negative adjusted with Cox regression model by breast cancer mortality risk factors in disease free survival and overall survival, respectively. Age and axillary lymph node

Table 3: Relative risk of mortality with disease free survival

Data	p-value	RR	95% CI for RR	
			Lower	Upper
Family	0.723	1.210	0.422	3.465
Estrogen	0.815	0.879	0.300	2.581
Progestron	0.663	0.794	0.281	2.243
P53_AG	0.850	1.093	0.437	2.734
C-ERB2	0.095	0.464	0.188	1.142
Menarche	0.443	0.889	0.659	1.201
Time of 1st pregnancy	0.097	1.092	0.984	1.211
Number of pregnancy	0.719	0.937	0.655	1.339
Age	0.017	0.928	0.873	0.987
Tumor size	0.131	1.751	0.846	3.624
Lymph node	0.000	1.934	1.351	2.769
Chemotherapy session	0.103	0.600	0.325	1.108

RR= Relative Risk

Table 4: Relative risk of mortality with overall survival

Data	p-value	RR	95% CI for RR	
			Lower	Upper
Family	0.414	3.243	0.193	54.463
Estrogen	0.520	2.494	0.154	40.280
Progestron	0.343	0.245	0.013	4.479
P53_AG	0.634	1.822	0.154	21.539
C-ERB2	0.787	0.697	0.050	9.627
Menarche	0.554	0.759	0.305	1.890
Time of 1st pregnancy	0.169	0.792	0.568	1.104
Number of pregnancy	0.440	0.723	0.317	1.647
Age	0.407	1.067	0.916	1.243
Tumor size	0.422	0.298	0.016	5.712
Lymph node	0.662	0.770	0.239	2.486
Chemotherapy session	0.203	0.234	0.025	2.187

RR = Relative Risk

involvement were the independent factors associated with relapse of neoplastic cells. The older age increased survival rate and decreased mortality (RR = 0.93 CI95% 0.87-0.99). In contrast, increase the number of involved lymph node increased mortality rate (RR = 1.93 CI 95% 1.35-2.77).

DISCUSSION

Of the 663 women diagnosed with breast cancer during follow-up, a total of 125 (19%) had a mother or a sister with breast cancer.

Other studies have shown that women with a family history of breast cancer had a 2-3-fold higher risk of breast cancer than did women without any affected family member, highest for those with a relative diagnosed before they were 50 years (Albrektsen *et al.*, 2006; Cauley *et al.*, 2006). Many studies have shown that family history is not a contraindication for breast conservative treatment and is not associated with a worse prognosis. Family history is not a prognostic factor for local recurrence rate in patients older than 40 years (Jobsen *et al.*, 2000). Present results did not indicate that the relationship between family history and survival of breast cancer. We adjusted both disease free and overall survival for family history with other risk factors.

According to analysis, family history was not a prognostic factor for breast cancer. However in some studies like Molino *et al.* (2004) have explained that the family history of breast cancer were younger at diagnosis (p = 0.002), had smaller tumours (p = 0.012), were more frequently estrogen receptor positive (p = 0.006) and diagnosed preclinically (p<0.001). It seems these controversial due

to expression of BRCA gene. There are some clear histopathological differences between BRCA1-related breast cancer and sporadic cases (more high grade, oestrogen receptor-negative and p53 positive tumours in BRCA1 mutation carriers), these differences are considered in prognosis of patients (Verkooijen *et al.*, 2006).

Margolin *et al.* (2006) did not observe a relationship between family history and phenotypic traits. Age and axillary lymph node involvement were the independent factors associated with relapse of disease in our findings. The other study in Iran also showed that tumor size and lymph node involvement were the important factors in the disease free survival and prognosis (Gohari *et al.*, 2006). One of the limitation of the current study was to not measure the BRCA gene in patients. However the previous studies have shown that the influence of family history on the prognosis of breast cancer is related to expression of BRCA gene.

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