RESEARCH COMMUNICATION

Population Based Survival of Female Breast Cancer Cases in Riyadh Region, Saudi Arabia

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Abstract

Breast cancer is the most frequent tumor among Saudi women, accounting to 19.8% of female cancers. The present study was conducted to determine 5-year survival for all cases of invasive breast cancer that occurred during 1994-96 in the province of Riyadh (n=316). The overall observed survival probability of the study population at 1, 3 and 5 years was 93.9%, 79.2% and 59.6%, respectively. The 5 year survivals for the younger (< 40 years), older (50 + years) and 40-49 years patients were 60.6%, 51.6% and 69.2% respectively, the differences not reaching statistical significance. While there was not a great deal of variation in the 5-year survival between cases with regional (55.6%), distant metastasis (57.6%) and extent of disease unknown (56.7%) cases, localized (67.5%) cases had a clearly better prognosis. An increased but not significant hazard was seen for the cases with regional and distant metastasis disease, 1.40 and 1.11 respectively, compared to localized cases. The 5-year survival for duct carcinomas (62.8%) was greater than for adenocarcinomas (55.6%) and lobular carcinomas (50.0%).

Key Words: Breast cancer - Population-based survival - Age - Extent of disease - Saudi Arabia.

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Introduction

The National Cancer Registry (NCR) in Saudi Arabia, functioning since 1994, collects data on cancer diagnosis by both active and passive methods. For ten years it has accumulated comprehensive and reliable population based incidence data on both malignant and in situ tumours. Data from the NCR show breast cancer to be the most frequent tumor among Saudi women, accounting for 19.8% of female cancers (Cancer Incidence Report, 2001). The age standardized incidence rate (14.1 per 100,000) is similar to the low rates found in most African and Asian populations. While population-based survival rates of cancer are useful in developing strategies for cancer service provision as well as cancer control programmes, the numbers of available estimates for developing countries are limited (Sankaranarayanan et al., 1999) and no such data have yet been published from Saudi Arabia. To overcome this deficiency, the present study was conducted to estimate breast cancer survival among Saudi patients living in Riyadh province.

Patients and Methods

The present study was based on the Saudi women living in the province of Riyadh with primary invasive breast cancer diagnosed between 1st January 1994 and 31st December 1996. The study cohort, consisting of 321 cases, was followed through 31st December 2002 for vital status (minimum of 6 years follow-up from the date of enrolment). Since there is no centralized mortality registering system in Saudi Arabia this was achieved by an active follow-up method. Based on the patients contact information (address/ telephone number) collected by the NCR, phone calls were made to the patients by a trained interviewer to elicit relevant information (e.g. vital status; cause of death, if patient was deceased). The same details were obtained by sending a reply paid letter to the patients for whom contact by phone was not possible. Also, for the non-responders of these methods or no other option to find out vital status, an attempt was made to collect last date of visit to hospital and condition of the patient at that time by scrutinizing medical records or computer systems containing follow-up information for these

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cases. Out of the 321 cases, 5 cases could not be traced for follow-up and were excluded from the study, leaving 316 (98.4%) cases as the total number of study subjects for the survival analysis.

The staging classification used in this report categorizes the breast cancer cases according to localized (confined to breast), regional (involvement of adjacent tissue/organ and/or positive regional lymph nodes), and distant disease (metastasis), the operational definitions used in the NCR based on the TNM staging manual. The histological categories of tumour used in this report were defined by International Classification of Diseases for Oncology, second edition (ICDO-2), WHO, 1990. They were grouped as duct carcinoma (ICDO code 8500), adenocarcinoma (codes 8140, 8141, 8480 and 8481), lobular carcinoma (codes 8520 and 8522) and 'others' (remaining ICDO codes). The overall observed survival, as well as stratified survival, were estimated by the Kaplan-Meier method (Kaplan and Meier 1958). Prognostic factors affecting the survival rate were predicted by applying the Cox (1972) proportional hazard model. The frequency distribution of variables and median survival period were obtained using EPI Info (Version 6; Centers for Disease Control and Prevention, Atlanta, US) software. All other analyses were performed using EGRET (Windows version 2.0; Cytel Software Corporation, US) software.

Results

Overall, information on vital status as on 31st December 2002 (complete follow-up) was available for 229 (72.5%) subjects, more than five year follow up information was available for a further 17 (5.4%) subjects and partial follow-up data (less than five year duration) were available for the remaining 70 (22.1%) subjects. The median follow-up period was 55.2 months. The mean age at diagnosis of the study population was 48.3 years (SD 14.5; range 24 to 93 years). A total of 98 (31.0%) cases were less than 40 years of age (mean 33.4 years; SD 3.8; range 24 to 39 years) and only 128 (40.5%) cases were in their 50s and above (mean 62.7 years; SD 10.3; range 50 to 93 years). The majority of the cases had duct carcinomas (69.6%) followed by adenocarcinomas (5.4%) and lobular carcinomas (4.7%). Almost equal numbers of cases had localized (96) and regional (102) disease. Further, extent of disease was unknown for 54 (17.1%) cases (Table 1). The frequency distribution of selected demographic and tumour related variables showed a major proportion (52-97%) of the cases to falls into the 'unknown' category for the following variables: marital status, subsite, histological grade and laterality (data not shown here).

The overall observed survival probabilities for the entire study population at 1, 3 and 5 years were 93.9%, 79.2% and 59.6%, respectively (Figure 1). The 5 year survival for the younger (< 40 years) and older (50 + years) group patients were 60.6% and 51.6%, respectively; a higher survival of 69.2% was observed for the age group 40-49 years (Figure 2). However, the best prognosis was observed for the age group 45-49 years with a 5 years survival of 78.2%. While there was not a great deal of variation in the 5-year survival between the regional (55.6%), distant metastasis (57.6%) and extent of disease unknown (56.7%) cases, the localized (67.5%) cases had better survival (Figure 3). Table 2 shows the distribution of extent of disease for the breast cancer cases by broad age groups with 5-year survival percentages. Each age group had approximately the same proportions of 'extent of disease unknown' cases and there was no significant variation in frequency among the age groups with respect to extent of disease. The 5-year survival for duct carcinomas (62.8%) was higher than for adenocarcinomas (55.6%) and lobular carcinomas (50.0%). To identify the independent effects of prognostic factors on survival, the Cox proportional hazards ratio was estimated only for the variables age at diagnosis, histology and extent of disease. However, in our study, none of these variables emerged as an independent predictor of breast cancer survival. The model identified an increased but not significant hazard (ratio of 1.34; 95% CI = 0.88 - 2.04) for the older age group (50 +

Table 1. Distribution of the Cases by Selected Characteristics

Characteristics	Number	Percentage
Age group		
< 40 years	98	31.0
40 - 49 years	90	28.5
50 + years	128	40.5
Extent of disease		
Localised	96	30.4
Regional	102	32.3
Distant metastasis	64	20.2
Unknown	54	17.1
Histological categories		
Duct carcinoma	220	69.6
Adenocarcinoma	17	5.4
Lobular carcinoma	15	4.7
Others	64	20.3

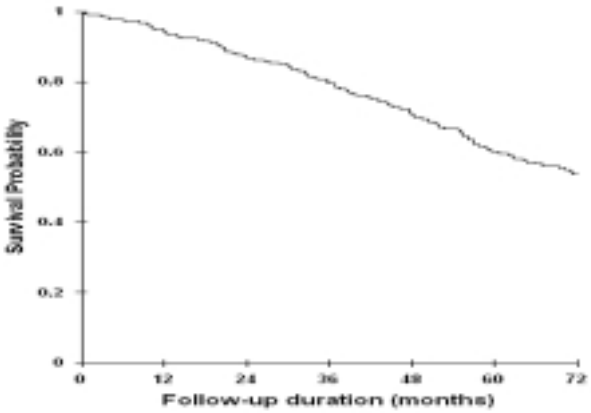

Figure 1. Kaplan-Meier Plot of Overall Survival for the Breast Cancer Cases from Riyadh Region, Saudi Arabia

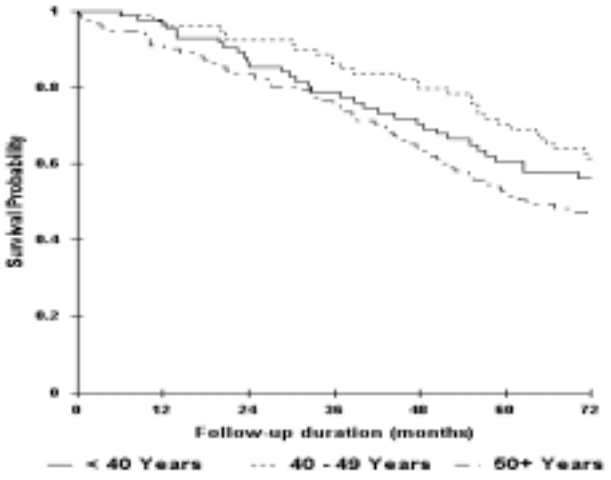

Figure 2. Kaplan-Meier Plot of Survival by Age Group for the Breast Cancer Cases from Riyadh Region, Saudi Arabia

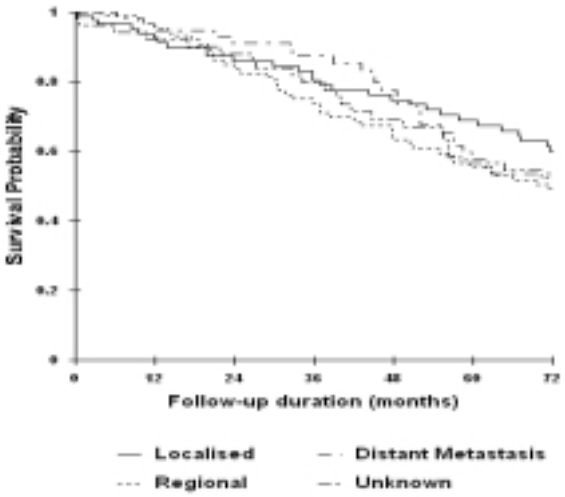

Figure 3. Kaplan-Meier Plot of Survival by Extent of Disease for the Breast Cancer Cases from Riyadh Region, Saudi Arabia

years) and a decreased non-significant hazard (ratio of 0.79; 95% CI= 0.49 - 1.28) for the 40-49 years age group compared to the younger age group (< 40 years). Similarly, an increased but not significant hazard was seen for the cases with regional and distant metastasis, 1.40 and 1.11 respectively, compared to localized cases (Table 3). Women with lobular carcinoma had an non-significantly higher risk (36%) than women with duct carcinoma.

Discussion

Two important goals of cancer surveillance are to provide milestones in the effort to reduce the cancer burden and to generate observations that can form the basis for cancer research and intervention for cancer prevention and control (Swan and Edwards 2003). Survival studies of cancer patients are essential for monitoring the effectiveness of cancer control programmes. The Kingdom of Saudi Arabia is divided into 13 administrative regions and the present study was based on one region that includes Riyadh, the capital city. About 27% of national breast cancer cases are from this region. In Saudi Arabia, with the country's improving socioeconomic profile, the health care social welfare schemes have developed rapidly since the 1970s and the Ministry of Health (MOH) predominantly provides health care services. The primary and secondary care is mostly provided by MOH with some participation by the private sector, particularly in urban areas. Several centres have been developed in the regions and in major cities such as Riyadh, Jeddah, and Dammam for cancer diagnosis and treatment. Other Ministries and institutions such as Ministries of the Interior and Defence, the National Guard and the King Faisal Specialist Hospital and Research Center are also involved in providing tertiary care in addition. Cancer diagnostic and treatment facilities have been widely developed in the country, although there are some discrepancies in their regional distribution, for example, for adiotherapy services. Surgery for common cancers is carried out in more than 50 hospitals, and cancer chemotherapy and paediatric oncology services are available in several centres as well.

The hospitals funded by the Ministries other than MOH are primarily for employees and their dependants. However, all the services provided by all the hospitals and institutions that are supported either by MOH or other ministries are free for nationals as well as for others working in the government sector, irrespective of their socio-economic status or educational level. There are currently no guidelines

Table 2. Distribution of the Cases by Extent of Disease and Age Group with 5 Year Survival Percentages

Extent of disease	< 40 years of age			40 - 49 years of age			50 + years of age		
	No. of cases	%	5 year survival	No. of cases	%	5 year survival	No. of cases	%	5 year survival
Localised	28	28.6	56.8	32	35.6	79.3	36	28.1	62.5
Regional	29	29.6	57.3	28	31.0	54.5	45	35.2	55.6
Distant metastasis	23	23.4	44.9	14	15.6	64.2	27	21.1	63.8
Unknown	18	18.4	87.5	16	17.8	73.3	20	15.6	12.0
Total	98	100.0	60.6	90	100.0	69.2	128	100.0	51.6

Table 3. Cox Proportional Hazards Ratio for the Variables Age at Diagnosis and Extent of Disease

Variables	Hazard Ratio	95% CI	P value
Age at diagnosis*			
< 40 years	1.00		
40 - 49 years	0.79	0.49 - 1.28	0.34
50 + years	1.34	0.88 - 2.04	0.17
Extent of disease			
Localised	1.00		
Regional	1.40	0.89 - 2.22	0.15
Distant metastasis	1.11	0.65 - 1.88	0.70

*: Significant (p = 0.049)

available to facilitate appropriate referral of suspected cancer patients from primary care for diagnosis and treatment. However, the access to any health care provided by the MOH will be of no problem for the nationals. Institutional guidelines for diagnosis and treatment of breast cancer are available in certain major hospitals in Saudi Arabia. For instance, such guidelines are available at the King Faisal Specialist Hospital and Research Centre (KFSH & RC), Riyadh. Efforts are currently being undertaken to develop one such on a national level for the management of breast cancer. However, the non-availability of such guidelines at other institutions preludes optimal treatment.

International differences in breast cancer survival rate exist (Gatta et al., 2000) and these differences are not easy to interpret. Longer survival in one country versus another may be due to the availability of better treatment, to similar treatments being more effective because diagnosis is made at an earlier stage of disease, or simply to early diagnosis without any advantage to the patient (lead-time bias) (Sant et al., 2004). The overall 5-year survival observed in this study was lower than in the U. S. and Europe (Sant et al., 2004) and higher than the developing countries (Sankaranarayanan et al., 1999). Though the present study is based on the incident cases diagnosed during 1994-96, while studies of developing countries are generally based on cases diagnosed during the early/mid 80s, the difference in survival cannot be explained fully by the incidence period effect mentioned by Sant et al (1991). The differences in breast carcinoma survival rate among European countries are attributable to differences in stage at diagnosis and treatment Sant et al (2003), whereas the survival differences in the U.S. appear due to race and socioeconomic status (Mariotto et al., 2002; Li et al., 2003), type of healthcare delivery (Potosky et al., 1997; Bradley et al., 2002) and type of health insurance (McDavid et al., 2003). However, actual differences could naturally reflect different patterns of care.

The effect of age at diagnosis on the prognosis of breast cancer is still controversial, although some studies (Brenner and Hakulinen 2003; Maggard et al., 2003) have shown a poorer prognosis for younger women. Rutqvist and Wallgren (1983) were able to demonstrate a far better survival for patients aged less than 50 years at diagnosis than those who were older. On the other hand, a study from Italy (Barchielli and Balzi 2000) showed age at diagnosis do not demonstrate any significant relation to 10-year relative survival. The survival advantage observed in our study for the patients aged 40 to 49 was similar to that shown by Sant et al (1991). Further, our finding that the women who were 45-49 years old had the best prognosis (5 years survival being 78.2%) was also observed among Swedish women (Adami et al., 1986). Also, the poorer survival observed in this study for the 50+ years patients than in other age groups was similar to the findings of Rutqvist and Wallgren (1983). However, it may be that the observed difference in survival with age merely reflects the fact that older women have a greater underlying risk of death, irrespective of breast cancer diagnosis.

The differences in survival observed here with extent of disease were not significant and the usual inverse relationship between survival rates and clinical extent of disease (Sankaranarayanan et al., 1999) was absent in our data. The exceptionally very high 5-year survival for the distant metastasis disease across all age groups suggests that these cases, most likely, contained a mixture of stages with a large proportion of localized and regional disease. Such misclassification of cases may either be due to inadequate/ non-availability of diagnostic facilities or inaccuracies in registration. Further, the higher 5-year survival observed for the 'extent of disease unknown' cases than for the group as a whole only in the two age groups (<40 and 40-49 years) suggests that information regarding extent of disease is not missing at random. Future studies are needed to confirm these phenomena. The fact of invasive lobular carcinoma having a poorer survival than that of invasive ductal carcinoma is in line with other studies (Ashikari et al., 1973; Mate et al., 1986). However, the statistical non-significance in survival difference by histologic type may be due to the low number of cases (15) of lobular carcinomas. Estimation of survival as well as hazard ratios for various variables other than age at diagnosis, histological types and extent of disease was not considered, as the proportions of 'status unknown' cases were too high (ranges from 52-97%) for any meaningful interpretation of the results. Appropriate adjustment for other known prognostic factors was not possible in this study to compare our survival data with those from other population-based case series. Nevertheless, the analysis led to several useful observations. Though the present study concerns women with breast cancer from one region, the results can be considered to reflect the country as a whole and the survival figures in this report, which describe the average fates of the patients diagnosed, can be used as reference values for monitoring cancer patients in Saudi Arabia as well as for evaluating the impact of cancer control activities on survival.

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