

RESEARCH ARTICLE

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Breast Cancer Diagnosis and Survival among Patients Diagnosed by a Structured Community Based Screening Program Compared to Opportunistic Diagnosis: A Case Control Study

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Abstract

Introduction: Breast cancer is ranked as the most common type of cancer effecting women worldwide. Early detection is associated with improved morbidity and mortality, along with decreased recurrence rates, due to regular breast cancer screening recommendations advised for women over the age of 40. Women in the Kingdom of Saudi Arabia (KSA) typically present with advanced symptoms at later stages due to lower-than-average rates of breast cancer awareness and screening. **Methods:** A case-control study was conducted utilizing data collected over 20 years in the primary care clinics linked to at a tertiary hospital to demonstrate the role of structured breast cancer screening programs within well-established primary care setting. Results were compared with outcomes of cancer cases diagnosed in the community through opportunistic diagnosis. **Results:** A total 292 patients included in the study had an overall mean survival time of 160 months, with a statistically significant higher survival time noted amongst the primary care group of 49 patients ($p < 0.01$) by approximately 85 months. Clinical stages and clinical response rates between the two patient groups were found to be statistically significant ($p < 0.01$), where 35 (73.3%) primary care patients were stage IIA and below, compared to 41 (30%) oncology patients. Patients who were diagnosed with breast cancer in the primary care group with well-established breast cancer screening programs were noted to present with breast cancer at earlier stages, have better prognosis and lower mortality as opposed to the oncology patient group. **Conclusion:** Our study highlights the need of structured breast cancer screening programs within well supported primary health services in Saudi Arabia and the region. Such programs were associated with improved survival outcomes and more favorable clinical responses. There is an urgent need to enable primary care services with the appropriate resources to significantly impact patient morbidity and mortality.

Keywords: Mammography- primary care- Saudi Arabia- prognosis- oncology

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Introduction

Breast cancer is the most common cancer amongst women in the Kingdom of Saudi Arabia, with an incidence of 14.8% and mortality rate of 8.5% of all cancer-related types within the last decade (Alqahtani et al., 2020). However, over half of all cases detected are at a later stage compared to a rate of 20% in other advanced countries (Ministry of Health of Saudi Arabia, 2022). Subsequently, this has led to a higher mortality rate as well as higher annual treatment costs compared to that noted in the United States, across all breast cancer stages (Alghamdi et al., 2021; Alqahtani et al., 2020; American Cancer Society, 2022b).

Similarly, breast cancer is the most common type of cancer diagnosed in women in the United States, accounting for approximately 30% of all new female cancer diagnoses each year and an incidence rate that increases by 0.5% each year. The American Cancer Society estimates that in the United States in 2022, about 280,000 new cases of invasive breast cancer will likely be diagnosed, of which about 43,000 will prove fatal (American Cancer Society, 2022c). Breast cancer has also been noted as the second leading cause of death due to cancer in women worldwide, although a steady decrease in mortality by 1% each year was noted between 2013 to 2018. This has been attributed to effective screening methods, increased awareness, and advancements in

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treatment regimens (American Cancer Society, 2022c).

Early breast cancer detection and treatment is known to improve morbidity and mortality (Saggu et al., 2015). As such, mammography is considered an important screening tool for breast cancer. Guidelines according to international entities (such as the U.S. Preventive Services Task Force, American Cancer Society and American Academy of Family Physicians) as well as the Ministry of Health of Saudi Arabia unanimously agree on yearly mammography screening in women aged 40 to 49 years with an average risk of breast cancer development (American Cancer Society, 2022b; Centers for Disease Control and Prevention, 2022). The American Cancer Society has established that average risk pertains to no personal or strong family history of breast cancer, no genetic mutation identified linked to greater risk of breast cancer (such as BRCA), and no history of chest irradiation prior to the age of 30. Women aged 55 years and older can choose to have mammograms conducted biannually instead and should continue screening if their overall health is good and have an estimated life expectancy of 10 years or more (American Cancer Society, 2022a).

The Ministry of Health of Saudi Arabia has established numerous awareness campaigns every year aimed at educating the general population on the screening methods and benefits of early breast cancer detection. In their published infographics, they explain how following simple tips such as undergoing a mammogram screening annually after the age of 40, earlier screening from the age of 30 if a history for breast cancer exists in the family and maintaining a healthy lifestyle can decrease the risk of breast cancer in women (Ministry of Health of Saudi Arabia, 2022).

This study aims to analyze the impact of a structured screening program using mammography in the diagnosis of breast cancer, through the evaluation of three key factors: the stage of breast cancer at diagnosis, overall survival, and disease-free period amongst breast cancer. These outcomes will then be compared with those found amongst patients diagnosed by opportunistic or hospital-based cancer detection modalities.

Materials and Methods

Study design and Setting

A case-control study was carried out in the primary care clinic at King Faisal Specialist Hospital & Research Center (KFSH&RC), a tertiary care teaching hospital in Riyadh, Saudi Arabia. The primary care clinics are run by board-certified consultants, providing a structured breast cancer screening program. The setting within KFSH&RC primary care clinics is highly digitalized, and the screening program is embedded within the health information system (HIS). It is based on the US Preventive Service Task Force (USPSTF) recommendation to conduct biennial mammogram screening in women aged 50 to 74 years. Patient records were obtained over a period of 20 years from January 2002 to February 2022.

Study participants

The catchment population is about 50,000 covered by

the primary care services of KFSH&RC. 20 board-certified primary care physicians are covering this catchment population.

All female patients over the age of forty diagnosed with breast cancer through the structured screening program at KFSH&RC were included in our study. The exclusion criteria were set as male patients and female patients already previously diagnosed with breast cancer.

This study included a total of 292 patients that were matched by comparing 1 patient from the primary care clinic with 5 patients from the oncology clinic matched by age and date of diagnosis.

Statistical methods

All statistical analysis of data was conducted using the software package SPSS, version 22 by IBM. Categorical variables were presented as frequencies and percentage, while continuous variables were expressed in means and standard deviations (SDs) with the level of statistical significance set at $p < 0.05$. Categorical variables were compared using the Chi-square and Fischer exact test, and the Kaplan Meier survival analysis with long rank test was used to assess the crude associations between breast cancer and its related risk factors. The date of last visit was used as the end date in Kaplan Meier analyses. In case the patient had passed away, the respondent or member of the family was asked to provide us with the date of death.

Results

A total of 292 female patients were included in the study; 49 patients were in the primary care clinic group and 243 in the oncology clinic group. 257 (88%) of all patients included were Saudi, and 26 (8.9%) non-Saudi residing in Saudi Arabia. The average age of all patients was 59.5 ± 8.6 years, with a mean number of 30.0 ± 47.3 months from diagnosis to death. At the first visit, 165 (56.5%) of all patients were at postmenopausal status, 127 (43.5%) at premenopausal status. The most frequent comorbidities were diabetes (28.1%), hypertension (26%), hyperlipidemia (12.7%), coronary artery disease (4.1%) and chronic kidney disease (2.1%).

Immediate and distant family history of cancer was noted in 7.5% and 1.4% of patients respectively. Clinical response was identified in 204 (69.9%) patients as complete remission, 1 (0.3%) in partial remission, 14 (4.8%) with stable disease, 57 (19.5%) with progressive disease and 5 (1.7%) unstable. Recurrence was also noted in 19 (6.5%) patients and metastasis in 63 (21.6%) patients. Status of last contact identified as 195 (66.8%) alive without breast cancer, 20 (6.8%) alive with breast cancer, 53 (18.2%) dead due to breast cancer, 5 (1.7%) dead due to other causes.

Clinical stages and clinical response rates between the patient groups were found to be statistically significant ($p < 0.01$) (Table 1). 35 (73.3%) primary care patients were stage IIA and below, compared to 41 (30%) oncology patients. 3 (6.1%) primary care patients had progressive cancer, compared to 54 (22.5%) oncology patients.

Table 1. Demographics and Clinical Characteristics

Variable		Family medicine group	Oncology group	P-value
Clinical stage	0	13 (27.1%)	6 (2.5%)	0.00*
	I	9 (18.8%)	30 (12.7%)	
	IIA	13 (27.1%)	35 (14.8%)	
	IIB	1 (2.1%)	36 (15.2%)	
	IIIA	5 (10.4%)	30 (12.7%)	
	IIIB	4 (8.3%)	45 (19.0%)	
	IV	3 (6.2%)	52 (21.9%)	
	Unstageable (U)	0 (0.0%)	3 (1.3%)	
Clinical response	Complete remission	45 (91.8%)	159 (66.2%)	0.019*
	Partial remission	0 (0.0%)	1 (0.4%)	
	Stable disease	0 (0.0%)	14 (5.8%)	
	Progressive disease	3 (6.1%)	54 (22.5%)	
	Not stable	0 (0.0%)	5 (2.1%)	
	Not applicable	1 (2.0%)	7 (2.9%)	
Patient comorbidity	Diabetes	15 (30.6%)	67 (27.8%)	0.69
	Hypertension	18 (36.7%)	58 (24.1%)	0.066
	Hyperlipidemia	12 (24.5%)	25 (10.4%)	0.007*
	Coronary artery disease	2 (4.1%)	10 (4.2%)	0.978
	Chronic kidney disease	5 (10.2%)	1 (0.4%)	0.001*

*Statistically significant

Survival Analysis

All the survival analysis results were found to be statistically significant ($p < 0.05$). An overall mean survival time of 160 months was found for all patients included in the study, with a statistically significant higher survival time noted amongst the primary care group of patients ($p < 0.01$) by approximately 85 months (Figure 1).

Discussion

Our study showed statistically significant differences in the clinical stage and response of the diseases between breast cancer patients diagnosed by a structured screening program within the primary care clinics and patients diagnosed and referred from the community to the oncology center, representing the oncology group. Most primary care patients (73%) presented at an earlier stage

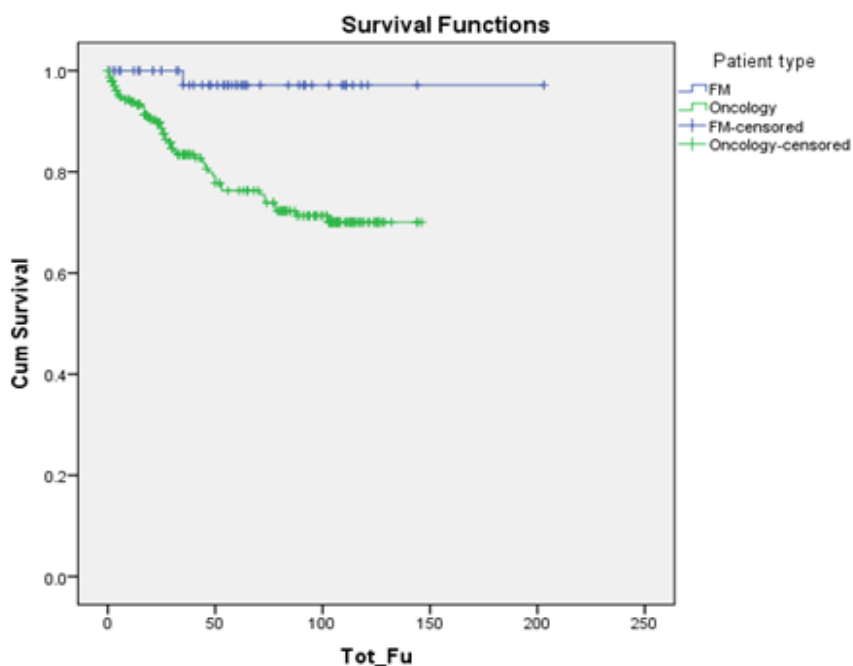


Figure 1. Means and Medians for Survival Time

($\leq 2A$), were less likely to progress to metastatic disease, and majority (91.8%) achieved complete remission. This is attributed to the structured mammography screening program within the primary care clinics allowing asymptomatic cancer to be detected at an earlier stage. Additionally, the benefit of beginning treatment at an earlier stage translated to less potential to metastasize, and less likely to recur.

In contrast, most patients who were referred from the community to the oncology center with breast cancer symptoms such as painful lump, abnormal discharge or swelling, were found to be at stage $\geq 2B$ at diagnosis. As such, our oncology group revealed a statistically significant lesser survival. This can be attributed to the fact that symptomatic breast cancer is more likely to present at a later stage.

Our study clearly demonstrates that patients who were followed up within the primary care clinics had a better prognosis. The primary care clinics at KFSH&RC has been well established, consisting of 30 board-certified consultants. Tools to aid physicians such as electronic medical records and decision supporting reminders facilitate physicians to do regular mammogram screening for patients on their healthcare check-ups.

In KSA, mammography was introduced prior to 2002, and a nationwide breast cancer screening center was established in 2007. Despite numerous efforts by the kingdom in increasing locations of primary care centers and providing health care services free of cost, studies have consistently raised concerns about the community access and knowledge about mammogram screening which resulted in lower uptake of mammogram screening by Saudi women compared to international screening rate (Akhtar et al., 2010; Al Mulhim et al., 2015; El Bcheraoui et al., 2015).

It is imperative to facilitate and improve screening rates for Saudi women, especially since most of them have a more advanced stage of disease and tumor size at first presentation compared to European and American women (Chouchane et al., 2013). Most mammography in the Arab world, and observed in our study, was opportunistic and diagnostic for concerns of breast lumps, swellings or discolorations.

Barriers to mammography have been investigated in a few studies. Among women, knowledge level about breast cancer and its risk factors has also been reported low. Access to mammography and incorrect beliefs about mammography were the most significant barrier to screening (Al-Zalabani et al., 2018; Alshahrani et al., 2019).

Primary care physicians, equipped with up-to-date information and standardized training, are in vast shortage in KSA (Al-Khaldi et al., 2017). Khalidi et al., (2017) found that primary care physicians constitute only 10% of physicians in primary care; general physicians (GPs) constitute and administer most of the primary care in the country. GPs in KSA commonly are medical graduates with no board qualifications or prior training and as such, are inadequately trained at providing healthcare at high standard levels. A small study done in 2014 revealed that only 19% of female GPs requested breast cancer screening

in women aged 40 and above (Saeedi et al., 2014).

Patient satisfaction is another factor impeding usage of primary care. Studies of local health services concluded that patients in Saudi Arabia were not satisfied with primary health care services (Alqossayir et al., 2021; Asiri et al., 2013). Most patients preferred bypassing primary health care centers and presenting to emergency rooms instead, which is not the standard setting for screening programs. The main reasons for dissatisfaction included shortage of trained healthcare professionals, lack of time for the providers, the physical environment, waiting times, the location of centers, and working hours.

In conclusion, breast cancer is the most common cancer amongst women worldwide, of which women in several countries present in later stages with a worse prognosis. Structured breast cancer screening programs, performed within well-established primary care services equipped with trained healthcare providers are important for early cancer detection to combat these rising breast cancer rates. This case-control study demonstrates improved survival outcomes of primary care patients in KSA using a structured breast cancer screening. This highlights the need to enable primary care centers with the appropriate resources to significantly impact patient morbidity and mortality.

Author Contribution Statement

All authors contributed, reviewed, and edited the manuscript.

Acknowledgements

Informed Consent

Not applicable.

Data availability

The authors declare that data supporting the findings of this study are available within the article.

Conflict of Interest

The authors declare no conflict of interest associated with this publication.

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