



Real World Data on Breast Cancer Survival in A Malaysian Cancer Centre

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Received: September 17, 2019; **Published:** October 17, 2019

Micro Abstract

In Malaysia, breast cancer is the most common cancer affecting women and is reported to have one of the lowest survival rates in the Asia Pacific region as of 2018. This study was undertaken to change the perception of public towards breast cancer survival rate in a cancer centre in Malaysia. Our findings demonstrated a favourable 5-year survival rate of 80.4%, compares favourably to survival data of developed countries.

Abstract

Real world data (RWD) is increasingly relevant in breast cancer (BC a) as it is the most frequently diagnosed cancer. Developed world has seen improved breast cancer survival, however, RWD on BC a survival in Malaysia is still lacking. This study aims to determine characteristics and survival of BC a patients from a single institute. Retrospective analysis of 168 BC a patients who were treated with at least one treatment modality in Beacon Hospital, Malaysia from 2008 - 2012 was conducted. Patient characteristics and treatments received were analysed descriptively to survival outcome. Vital status was obtained from the National Registry of Birth and Death (NRD) records. Observed survival rates were estimated by Kaplan-Meier method and difference between groups by log-rank. Of 143 eligible BC a patients, 28 (19.6%) died during the study period. Five-year BC a specific survival rates were 100% for Stage I and II, 79.31% for stage III and 38.89% for Stage IV disease. In the multivariate analysis, higher stage at diagnosis, triple negative breast cancer with metastases and higher grade were associated with worse survival outcomes. The overall 5-year survival rate of BC a patients in Beacon Hospital from 2008 - 2012 compares favourably to the survival data of developed countries.

Keywords: Breast Cancer; Survival Outcome; Real World Data; Malaysia; Triple Negative Breast Cancer; 5-Year Survival of Breast Cancer

Introduction

Breast cancer is the most common cancer affecting Malaysian women and is the most common cancer-related mortality in women worldwide [1]. The breast cancer incidence and survival rates were reportedly lower in Eastern Asia in contrast to developed

countries. Besides, recent Asian studies indicated that the annual incidence of breast cancer have doubled over the past two decades [2,3]. though studies from the Western countries have reported otherwise [3,4].

Breast cancer has a high survival rate when detected early and given appropriate treatment [5]. Despite the dramatic variation between populations [6], generally, breast cancer patient outcomes have improved substantially over the years. Currently, age standardized relative survival at 5 years is recorded at > 80% for developed countries including Japan, North America, Sweden, Finland and Australia, in contrast to developing countries, where 5-year survival rates are recorded at < 40 - 60% [7].

To further understand the disease epidemiology and survival rates with respect to patient characteristics, treatment options and outcomes, observational studies are fundamental in providing valuable information. Real world data (RWD) is increasingly gaining attention for its pivotal role in health care related planning of diseases, particularly for breast cancer as it poses significant burden for women in Asia with reportedly the highest number of breast cancer cases (53%) up to 2012 [8]. However, RWD on breast cancer and treatment outcomes remains limited in Malaysia to date. This study aims to describe patient characteristics and survival in real-world and to report improvement in 5-year overall survival of breast cancer using data obtained from Beacon Hospital, formerly known as Beacon International Specialist Centre (BISC), a private healthcare centre in Malaysia.

Materials and Methods

Study population

We conducted a retrospective observational cohort study by examining the data on pathologically confirmed primary breast cancer patient who had received at least one treatment modality at Beacon Hospital, Petaling Jaya, Malaysia. All 168 breast cancer patients diagnosed from 1st of January 2008 to 31st of December 2012 were reviewed for this study. Identification of case was done through hospital registry with further data retrieved from past chemotherapy, radiotherapy records. Foreign patients, patients with non-epithelial malignancy or recurrent tumour were excluded from this study.

Data collection

Medical records as well as patient's histopathology reports (HPE) were extracted. Patient demography to include age, ethnicity and nationality; tumour characteristics to include size, grade, hormonal receptor status and staging; treatment patterns and survival were analysed descriptively. Staging of the disease was based on the American Joint Committee on Cancer (AJCC) criteria. The survival data of the patients at the end of the study period and the date of death were obtained from the medical records / National

Registry of Birth and Death (NRD). Ethics approval is obtained from Medical Research Ethics Committee (MREC ID: NMRR-11 – 38 - 2814).

Statistical analysis

Statistical analyses were performed using Med Calc. The patient's characteristics were described by percentages. Kaplan-Meier analyses were conducted to estimate overall survival rates. The survival time of a patient is referred to the number of months from the date of diagnosis to the date of the death or the date of last follow-up. Log-rank test was used to compare survival distributions of different subgroups in our data. Two tailed p value of < 0.05 was considered statistically significant.

Results

Data from 168 patients were gathered for this study, of which only 143 were eligible for this study. Malaysian Chinese comprises 59.4% of the total patients, 32.1% were Malay and 7.7% were Malaysian Indians. Only 1 patient is from other ethnic groups. Patient demographic is presented in table 1. The age of diagnosis was recorded from the first admission. The mean age of diagnosis was 53 years, with the youngest age of diagnosis recorded at 23 years. When categorized by stage, 22/36 (61%) stage 4 patients were in menopausal age. Most of the patients presented with early breast cancer (52.7%). The major histological subtype among patients was invasive ductal carcinoma (IDC), which makes up 86% of cases during the study period. In addition, most of the patients (59.4%) were diagnosed with moderate to large tumour size (\geq T2). 100/143 (69.9%) of the enrolled patients were oestrogen receptor positive; 83/143 (58%) were progesterone receptor positive; 42/143 (29.4%) were HER2 positive; and 17.5% were Triple Negative.

Characteristics	Patients (n=143)
Age	
Median (range)	51 (23 - 95)
Ethnicity, n (%)	
Malay	46 (32.2)
Chinese	85 (59.4)
Indian	11 (7.7)
Other	1 (0.7)
ECOG/PS, n (%)	
0	46 (32.2)
1	16 (11.2)
\geq 2	5 (3.5)

Unknown	76 (53.2)
Stage at presentation, n (%)	
IA-IB	26 (18.2)
IIA-IIB	49 (34.3)
IIIA-IIIC	29 (20.3)
IV	36 (25.2)
Tumour size, n (%)	
T1 (≤20mm)	58 (40.6)
T2 (20<T≤50mm)	67 (46.9)
T3 (<50mm)	8 (5.6)
Unknown	10 (7.0)
Regional nodes, n (%)	
Negative	69 (48.3)
Positive	63 (44.1)
Unknown	11 (7.7)
Tumour histology, n (%)	
Invasive breast carcinoma	132 (92.3)
IDC	123 (86.0)
ILC	8 (5.6)
Mixed IDC/ILC	1 (0.7)
Ductal carcinoma in situ	3 (2.1)
Other carcinomas	5 (3.5)
Unknown	3 (2.1)
Grading, n (%)	
1	8 (5.6)
2	58 (40.6)
3	61 (42.7)
Unknown	16 (11.2)
Hormonal receptor status, n (%)	
ER - and PR -	38 (26.6)
ER + and/or PR+	102 (71.3)
HER2	42 (29.4)
Triple Negative	25 (17.5)
Unknown	9 (6.3)
Site of Metastasis, n (%)	36
Lung	14 (38.9)
CNS	12 (33.3)
Bone	24 (66.7)
Liver	16 (44.4)
Others	10 (27.8)
Unknown	1 (2.8)
Only 1 visceral organ	16 (44.4)
>1 visceral organ	6 (16.7)

Table 1: Patient demographic for breast cancer patients (2008-2012) in BISC.

From the 129 patients who underwent surgery, about half (51.5%) of the patients underwent mastectomy and 37.8% opted for lumpectomy. For metastatic breast cancer patients, less than

half (44.4%) of the patients were undergoing first line chemotherapy, whereas 19.44% were on their second line chemotherapy with the remaining (27.8%) had already received more than 2 lines of chemotherapy. Moreover, 7.5% of early stage or locally advanced breast cancer patients refused treatment whereas 11.1% of advanced stage patients refused palliative treatments. Meanwhile, 21.43% of patients (from both early stage and advanced stage) refused trastuzumab treatment despite diagnosed with HER2 positive. See table 2 for treatment patterns amongst breast cancer patients who sought treatment at Beacon Hospital.

Treatment modalities	Early/ Locally Advanced (n=107)	Metastatic Breast Cancer (n=36)
Radiotherapy, n (%)	95 (88.97)	31 (86.11)
<i>Site</i>		
Breast/Wall	89 (93.7)	15 (51.6)
Others	6 (6.3)	16 (48.4)
<i>Treatment regime</i>		
Curative intent	88 (92.6)	
Palliative intent	6 (6.3)	
Unknown	1 (1.1)	
Systemic Therapy, n (%)	107 (100)	35 (97.2)
Chemotherapy, n (%)	88 (82.2)	33 (94.3)
Neo-adjuvant	2 (2.3)	
Adjuvant	82 (93.2)	
Neo-adjuvant and adjuvant	3 (3.4)	
Unknown	1 (1.1)	
Hormonal Therapy, n (%)	77 (71.96)	21 (60)
Oestrogen Receptor Antagonist Tamoxifen	57 (74.0)	11 (31.4)
<i>Aromatase Inhibitor</i>		
Letrozole	16 (20.8)	12 (34.3)
Anastrozole	16 (20.8)	8 (22.9)
Exemestane	3 (3.9)	6 (17.2)
GnRH ag (Goserelin Acetate)	4 (5.2)	2 (5.7)
Progestogens	0	0
Anti-androgens	0	0
Leuprorelin Acetate	0	1 (2.9)
Targeted Therapy, n (%)	22 (28.6)	14 (40)
Trastuzumab	22 (28.6)	11 (31.4)
Pertuzumab	0	0
Trastuzumab-emtansine	0	2 (5.7)
Lapatinib	2 (2.6)	11 (31.4)
No Treatment, n (%)		
HER2 positive	6 (21.4)	3 (21.4)
All types	8 (7.5)	4 (11.1)

Table 2: Treatment patterns for breast cancer patients stratified by disease stage.

The overall 5-year survival rate was 80.4%, with a median overall 5-year survival of 75.93 months (95% CI: 73.034 - 83.546). Twenty-eight (19.6%) breast cancer patient died during the study period. The overall survival was 100% at 5 years for both Stage I and stage II, 79.31% for stage III and 38.89% for Stage IV disease (Figure 1A (i)) ($p < 0.0001$).

The 5-year survival rates amongst three main ethnic groups observed that the Indian women recorded the highest survival rate (81.82%), followed by Chinese women (81.18%) and Malay (78.26%) (Figure 1A(ii)) though not statistically significant ($p = 0.9604$). We have also failed to detect any association between survival and age of diagnosis ($p = 0.493$). In addition, our study has found that stage 4 patients in the > 50 years age group has a

better overall survival (40.91%) when compared to patients from the younger age group (28.57%), however the difference is not statistically significant ($p = 0.9796$). We also further stratified stage 4 patients by their hormonal status, particularly ER, and found that the survival outcome is similar (ER negative: 33.3% and ER positive: 37.5%) regardless of their ER status ($p = 0.9831$) Figure 1B.

On the other hand, we also investigated the survival outcome of the patients with triple negative breast cancer subtype, categorized by their metastasis status. Our study reported a 100% 5-year overall survival in triple negative breast cancer patients without presence of metastasis, whereas triple negative breast cancer patients with the presence of metastasis recorded a 40% survival ($p = 0.0004$). (Figure 1C).

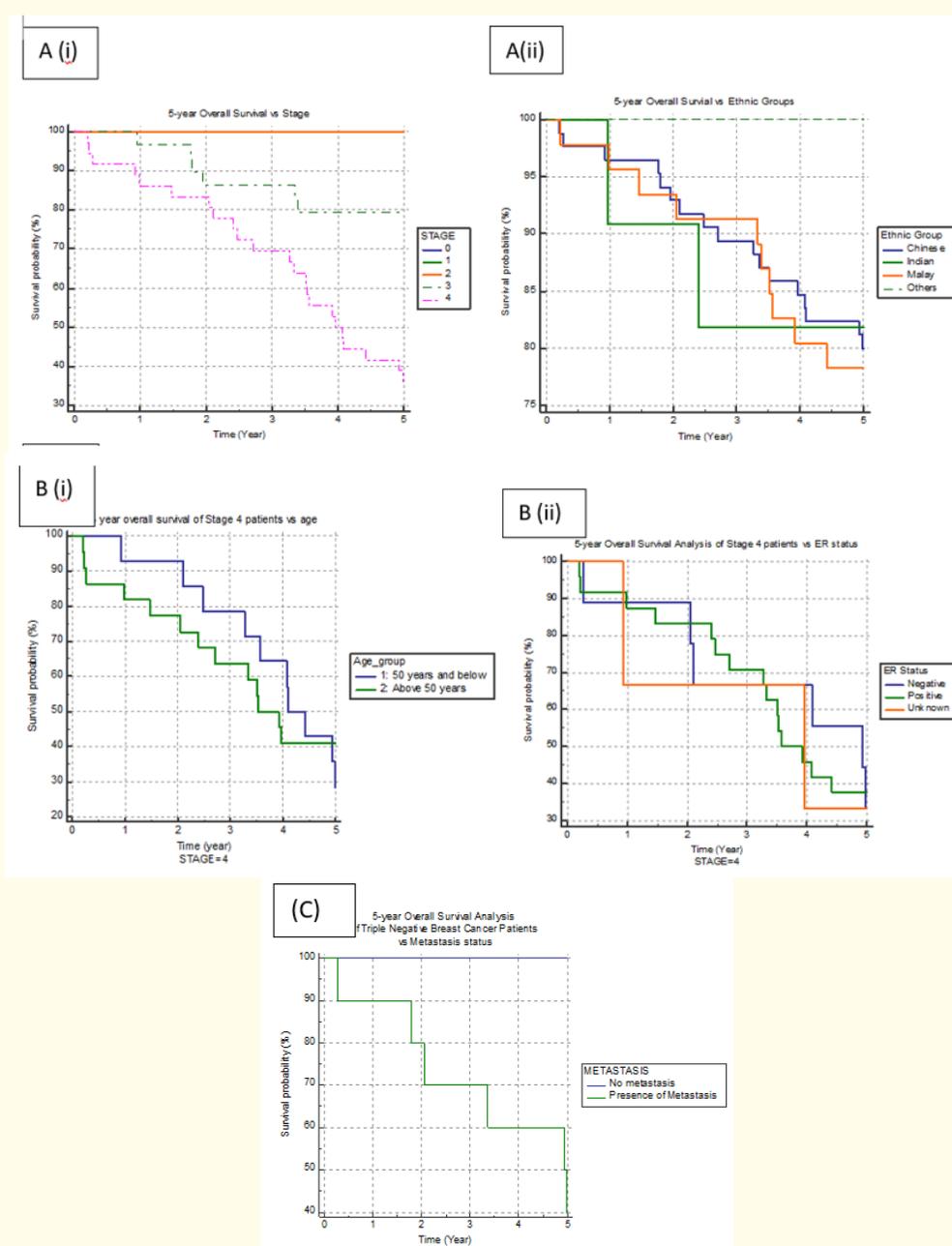


Figure 1: Kaplan-Meier 5-year Overall survival analysis. 5-year survival analysis of breast cancer patients stratified by (A(i)) stage, (A(ii)) ethnicity; 5-year survival analysis of Stage 4 breast cancer patients stratified by (B(i)) age; (B(ii)) ER status; (C) 5-year overall survival analysis of breast cancer patients with triple negative subtype stratified by status of metastases. Triple negative patients without the presence of metastasis has a significantly better survival in contrast to those with the presence of metastases ($p=0.0004$).

Discussion

Breast cancer survival data are lacking in Malaysia. To date, there are only 3 institutional-based and one populational based studies were conducted within the country [9-11]. Although breast cancer rates remain comparatively low amongst Asian women, a large body of scientific literature supports the notion that the breast cancer incidence has increased at an alarming rate in Asia [12,13]. In addition, a higher mortality-to-incidence ratio, more aggressive disease at diagnosis and reduced survival were also observed in less developed countries when compared to more developed countries in Asia [14]. Therefore, RWD is pivotal not only at providing an overall view on the breast cancer disease outcome and survival rate, but also to evaluate the effectiveness of treatment plans in a healthcare setting and to gain public confidence on cancer treatment in our country. In the current study, we evaluated the 5-year overall survival rate of breast cancer patients using data from a single institution. The evaluation of a healthcare centre's cancer care performance is relatively new in Malaysia, and this is especially true amongst Malaysian private healthcare centres.

Studies in the past have revealed a lower 5-year overall survival in Asian countries (below 40%) compared to developed countries (> 80%). The current study, however, observed a high 5-year overall survival rate of 80.42% for breast cancer patients from Beacon Hospital. Our finding is in concordance to another single-centre cohort from University of Malaya Medical Centre (UMMC) which have reported an improvement of survival from 58% to 76% for patients diagnosed in 1993 -1997 compared to 1998-2002 [15]. In fact, our findings on survival rate is similar to the combined report from National University Hospital Singapore (NUHS) and UMMC, which revealed a 5-year overall survival of 30.2% for stage III and IV patients [9].

It is generally well accepted that breast cancer rates differ substantially across different ethnic groups. White Americans and Black Americans were reported to have a higher breast cancer incidence rate when compared to Hispanic women and Asian women. The same findings have also been demonstrated on Malaysian women, comprising of the 3 most populous ethnic groups in Asia, where Malay women were reported to have significantly higher risk of all-cause mortality, independent of age, stage, tumour characteristics and treatment compared to Indian and Chinese ethnic group [11,16]. However, the current study did not find significant disparity in the 5-year overall survival when patients were compared by ethnic groups. Similarly, when patients were

categorized by age groups, there was no significant difference in the 5-year overall survival. This is in contrast to previous findings, where post-menopausal patients were observed to have better survival whilst younger patients tend to have poor survival [17,18].

Triple-negative breast cancer (TNBC) is a sub-category of breast tumour which lacks the expression of the three most commonly targeted biomarkers considered for breast cancer treatment, namely oestrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor (HER2) [19]. TNBC accounts for 15-20% of all breast cancer diagnoses and is usually associated with more aggressive clinical course, worse evolution within the first 3 to 5 years after diagnosis; early and higher rates of distant visceral metastasis compared to other breast cancer subtypes, as well as poor survival [19-22]. As the TNBC subtype is commonly associated with poor prognosis, the present study evaluated the 5-year overall survival of this group of patients and reported a 76% 5-year overall survival, with the mean time to death of 4.5 years (4.015 to 4.977). This is in concordance to previous findings which reported a 68% - 82% 5-year survival for TNBC patients [23-25]. TNBC patients are four times more likely to develop visceral metastases in contrast to non-TNBC subtype [26]. In addition, the treatment decision for metastatic TNBC is also challenging due to the lack of targeted therapy. Therefore, we also further evaluated the 5-year overall survival of TNBC patients based on the presence of metastasis. Here, TNBC patients without metastasis recorded a 100% 5-year overall survival, in contrast to only a 40% survival for those with the presence of metastases. The finding from this study compares favourably to studies conducted in Taiwan and Peru which reported a 26.5% and 26% 5-year OS for TNBC patient with metastasis respectively [27,28]. In support of this notion, another study from the US has also reported greater than 75% breast cancer-specific mortality for TNBC patients who experienced distant recurrence [29].

One obvious limitation of this study is that this is a single-institution-based studies and that the small number of patients investigated could not be a representation of the management and outcome of breast cancer in Malaysia. The small number of patients have also limited the statistical power of some analyses and were insufficient to reach definitive conclusions. We were also not able to evaluate the influence of covariates such as the histopathology subtypes, the presence of hormone receptors and the type of treatment on the survival rate. In addition to that, it is difficult to determine the direct or indirect cause of death related to breast cancer.

Despite these limitations, this study provides an encouraging RWD result on breast cancer survival for a relatively new cancer centre in Malaysia.

In conclusion, the overall 5-year survival rate of breast cancer patients amongst Malaysian women who sought treatment in Beacon Hospital from 2008 - 2012 compares favourably to the survival data of North America and Oceania at 84%. Findings from the present study will be useful in assisting advocacy organisations to provide information about resources and support as well as to raise awareness.

Clinical practice points

Although breast cancer incidence rates remain low in Asian countries, it is however reported to have the lowest five-year survival rates in contrast to developed countries. At present, Malaysia is reported to have a five-year survival rate of only 49% for breast cancer, recorded as one of the lowest survival rates in the Asia Pacific region, in contrast to 92% in South Korea, 83% in Singapore, over 60% in China and 52% in India [30]. It has been suggested that the low survival rate is primarily attributed to the late presentation of the disease and poor adherence to treatment recommendations [31]. As breast cancer survival data remains under reported in Malaysia to this date, the present study revealed an updated institutional survival data which compares favourably to Western countries. Although this data is not adequate to represent the survival rate of the entire nation, we deem it pivotal to be served as a benchmark from a hospital that focuses primarily in cancer treatment and management. This study also serves to advocate the importance of early detection as breast cancer patient presented at early stage (Stage I and II) recorded a 100% five-year survival at our institution. Understanding the treatment modalities pattern and analysing it simultaneously to survival rate shed light to the public on the importance seeking treatment for breast cancer as early as possible while adhering to recommended treatments.

Acknowledgements

We thank the Medical Records department from Beacon Hospital for facilitating the medical records retrieval and tracing the present status of the patients.

Funding Sources

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflicts of Interest

All authors have declared no conflict of interest.

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Volume 3 Issue 11 November 2019

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