Data Analysis of Survival Outcome of Breast Cancer Patients at Department of Oncology Faculty of Medicine Ain Shams University, Retrospective Study

Thesis

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*in **Clinical Oncology & Nuclear Medicine***

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بسم الله الرحمن الرحيم

وَقُلِ اعْمَلُوا فَسَيَرَى اللَّهُ
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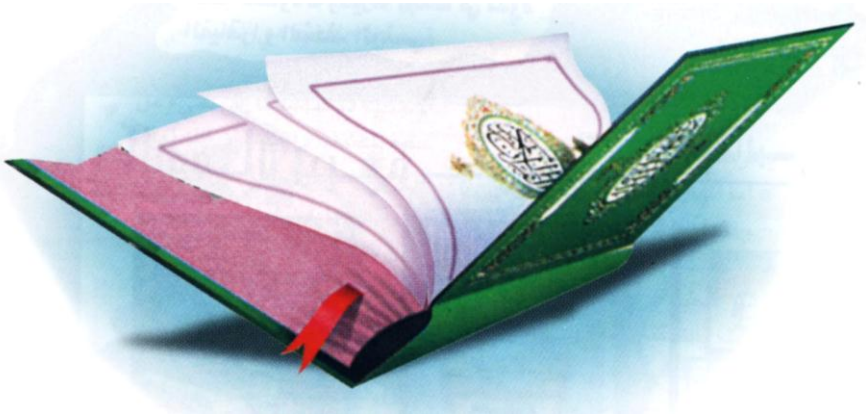

صدق الله العظيم

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Ahmed Mohamed El-Shafei Shams

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List of Abbreviations

Abb.	Full term
ACS	*American cancer society*
AJCC	*American Joint Committee on Cancer*
BBD	*Benign breast disease*
BC	*Breast cancer*
BCAC	*Breast Cancer Association Consortium Studies*
BMI	*Body mass index*
BOADICEA	*Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm*
BSE	*Breast self-examination*
CBCS	*Carolina Breast Cancer Study*
CBE	*Clinical breast examination*
CHEK2	*checkpoint kinase 2*
CI	*Confidence interval*
CK5/6	*Cytoeratin 5/6*
CTC	*Circulating tumor cells*
DCIS	*Ductal carcinoma in situ*
DFS	*Disease free survival*
ER	*Estrogen receptors*
GPBCR	*Gharbia Population based Cancer Registry*
HBEGF	*Heparin-binding epidermal growth factor-like growth factor*
HBOC	*Hereditary breast and ovarian cancer syndrome*
HGF	*Hepatocytegrowth factor*
HR	*Hazard ratio*
HRT	*Hormonal replacement therapy*
HT	*Hormonal therapy*
IHC	*Immunohistochemistry*
LCIS	*Lobular carcinoma in situ*
LVI	*Lympho vascular invasion*
MOP	*Monoparity*

List of Abbreviations cont...

Abb.	Full term
MP	*Multiparity*
MRI	*Magnetic resonance imaging*
NCCN	*National comprehensive cancer network*
NCI	*National cancer institute*
NCRPE	*National Cancer Registry Program*
NP	*Nulliparity*
NSABP-P1	*National Surgical Adjuvant Breast and Bowel Project Study*
OCP	*Oral contraceptive pills*
OR	*Odds ratio*
OS	*Overall survival*
PBCS	*Polish Breast Cancer Study*
PBM	*Prophylactic bilateral mastectomy*
PBSO	*Prophylactic bilateral salpingo-oophorectomy*
PE	*Pulmonary embolism*
PFS	*Progression free survival*
PR	*Progesterone receptors*
RANKL	*Receptor activator of NF-kappa B ligand*
RR	*Relative ratio*
SERMs	*Selective estrogen receptor modulators*
STAR P-2	*Study of Tamoxifen and Raloxifen*
TN	*Triple negative*
US	*United States*
USPSTF	*United States Preventive Service Task Force*
VEGF	*Vascular endothelial growth factor*
WHI	*Women's Health Initiative*
WHO	*World health organization*
WINS	*Women's Intervention Nutrition Study*

INTRODUCTION

Breast cancer is the most common cancer among females worldwide, and the second most common cause of cancer related death after lung cancer, which makes its global burden substantial. However, the burden is not evenly distributed worldwide: with large variations between different countries, regions, and within specific regions ***(Hortobagyi et al., 2005).***

BC patients with the same stage of disease can have markedly different treatment responses and overall outcome. The strongest predictors for prognosis (for example, lymph node status and histological grade) fail to classify accurately breast tumours according to their clinical behaviour, Chemotherapy or hormonal therapy reduces the risk of distant metastases by approximately one-third; however, 70–80% of patients receiving this treatment would have survived without it ***(Laura et al., 2002).***

Adjuvant systemic therapy substantially improves disease free survival (DFS) and overall survival (OS) in both premenopausal and postmenopausal women up to the age of 70 years with lymph-node–negative or lymph-node–positive BC ***(Marc et al., 2002).***

The causes of this observed survival difference are likely multifactorial and include socioeconomic factors, differences in access to screening and treatment, as well as potential

biological differences among the cancers themselves. Biological differences among BC may reflect genetic influences, differences in lifestyle, or nutritional or environmental exposures ***(Lisa et al., 2006).***

Appropriate systemic therapy of BC generally requires knowledge of Estrogenic Receptor (ER), Progesterone Receptor (PR), and Human epidermal growth factor receptor 2(HER 2 neu). Endocrine sensitivity, assessed by the expression of ER and/or PR has long been recognized as a predictive factor for response to hormonal treatment. Similarly, HER2 overexpression is useful for selecting targeted anti-HER2 therapy. Until recently, most studies reported BC as endocrine responsive (ER and/or PR positive) and separately reported the status of HER2 ***(Carol et al., 2009).***

The choice of treatment strategy must be extensively discussed with the patient and take into account the patient's preferences, It should be based on the tumour burden/location (size and location of primary tumour, number of lesions and extent of lymph node involvement) and biology (pathology, including biomarkers and gene expression), as well as the age and general health status of the patient ***(Senkus et al., 2015).***

Prognostic factors that are considered to be independent variables include lymph node status, tumor size, grade, presence of lymph-vascular invasion, age and tumor proliferation markers. Certain biologic factors, including ER,

PR and HER2 neu, are both prognostic and predictive factors ***(Cianfrocca et al., 2004).***

Long-term survival rates after diagnosis of BC are steadily rising. This is good news, but clinicians should also recognize that this brings new challenges to the medical community. As BC becomes a chronic condition rather than a life-threatening illness owing to advances in early diagnosis and more effective treatments ***(Perm et al., 2015).***

Despite the predictive power of intrinsic BC phenotypes, such as luminal, basal, and HER2, extent of disease also offers predictive synergy. The anatomic TN M classification provides a common language for communicating disease burden ***(Giuliano et al., 2017).***

AIM OF THE WORK

Assessment of disease free survival and oval all survival of BC patients in relation to treatment which was received in each group of the population at department of oncology faculty of medicine Ain Shams University.

Chapter 1:

EPIDEMIOLOGY AND RISK FACTORS

Incidence and Mortality:

Global cancer statistics show that BC is the most frequently diagnosed cancer and the second leading cause of cancer death among females, accounting for 23% of total cancer cases and 14% of cancer deaths ***(Smith et al., 2017).***

The chance that a woman will die from BC is about 1 in 38 (about 2.6%), death rates from female BC dropped 39% from 1989 to 2015. Since 2007; BC death rates have been steady in women younger than 50, but have continued to decrease in older women, these decreases are believed to be the result of finding BC earlier through screening and increased awareness, as well as better treatments ***(Smith et al., 2017).***

Incidence of BC varies greatly between different countries in the world. The incidence is higher in developed countries and lower in developing countries. Yet, immigrants to high developed countries gain the same high risk and higher incidence of BC exactly like habitants of high developed countries, not like their original countries ***(Hoel et al., 2006).***

In Egypt, according to data of the National Population-Based Cancer Registry Program, BC is the most common female cancer; it comprises about 32% of malignancies in females ***(Ibrahim et al., 2014).***

Risk factors

1- Female gender:

BC occurs 100 times more frequently in women than in men. In the United States, over 200,000 women are diagnosed with invasive BC each year, compared to approximately 2000 cases that occur annually in men ***(DeSantis et al., 2013).***

2- Age:

According to data from the Surveillance, Epidemiology, and End Results (SEER) database, the risk of BC increases with older age and peaks in the sixth decade ***(Jemal et al., 2011).***

3- Menarche and the menstrual cycle:

Younger age at menarche and/or later age at menopause are associated with a higher risk of BC **(*Colditz and Rosner, 2000).***

The risk is reduced by about 5% for each 1 year later in starting menstruation and the association between age of menarche and risk of BC is more evident at premenopausal females of younger age ***(Huang et al., 1997).***

4- Childbearing and Nulliparity:

BC risk is elevated immediately after delivery and this risk is lowered in the years following that, up to the point that there is a protective effect of giving birth against BC ***(Beral et al., 2004).***

This protective effect is evident among women who have at least one full term pregnancy, these women have a reduction in BC risk by about 25% compared to nulliparous women; The more the full term pregnancies, the more the protective effect is evident, women who have at least five full term pregnancies have a 50% lower risk of BC versus nulliparous women ***(Layde et al., 1989).***

The age at first full term pregnancy influences the risk of BC independently of the total number of pregnancies; protection is higher related to the younger the age at first birth ***(Kelsey et al., 1993).***

Women who had first birth when being younger than 20 years had a 30% reduction in the risk of BC compared to those with a first birth after the age of 35 ***(Ewertz et al., 1990).***

Evidence about incomplete pregnancies, is less clear, but suggests that there is no large effect on BC risk ***(Kelsey et al., 1993).***

Factors that increase the number of menstrual cycles also increase the risk of BC, probably due to increased endogenous