Retrospective Analysis for the Impact of Adjuvant Chemotherapy Initiation Timing On The outcome of Non Metastatic Breast Cancer at Ain Shams Hospitals

Thesis

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Asmaa Waheed Mohammed Mostafa

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List of Abbreviations

Abb.	Full term
AIs	Aromatase inhibitors
AJCC	American Joint Committee on Cancer
ALND	Axillary lymph node dissection
APBI	Accelerated partial breast irradiation
ASTRO	American Society for Radiation Oncology
BCS	Breast conservative surgery
BI-RADS	Breast Imaging Reporting and Data System
CNB	Core needle biopsy
CT	Computed tomography
DCIS	Ductal carcinoma in situ
DFS	Disease-free survival
DMFS	Distant metastasis-free survival
ER	Estrogen receptor
FNAB	Fine Needle Aspiration Biopsy
HER2	Human epidermal receptor
HR	Hormone receptor
IDC	Invasive ductal carcinoma
ILC	Invasive lobular carcinoma
LCIS	Lobular carcinoma in situ
LNR	Lymph node ratio
LVI	Lymphovascular invasion
MRM	Modified radical mastectomy
NCCN	National Comprehensive Cancer Network

List of Abbreviations (Cont...)

Abb.	Full term
NSABP	National Surgical Adjuvant Breast and Bowel Project
OC	Oral contraceptives
OS	Overall survival
PET	Positron emission tomography
PR	Progesterone receptors
SEER	Surveillance, Epidemiology, and End-Results
SERMs	Selective estrogen receptor modulators
SLNB	Sentinel lymph node biopsy
SRI	Surgery radiotherapy interval
TNBC	Triple negative breast cancer
TNM	Tumor, node, metastasis classification
TTC	Time to chemotherapy
WHO	World health organization

ABSTRACT

Breast cancer is the most commonly diagnosed cancer and the leading cause of cancer deaths in women worldwide, accounting for 23% of total cancer cases and 14% of all cancer related mortalities. This study is a retrospective analysis conducted over 300 female patients diagnosed with invasive non metastatic breast cancer presented to Clinical oncology department at Ain-Shams University hospitals. All patient's records in the period from January 2007 to December 2011 were reviewed allowing five years overall survival and disease free survival follow up, all these data were collected through chart analysis. Patient characteristics, clinical picture and pathological data were thoroughly collected. In the current study, many of the parameters addressed were almost similar to worldwide incidences with little variations. Mean age at diagnosis was 50 years. Stage II was the most prevalent stage, IDC was the most common pathological subtype, and the hormone receptor positive was the most common molecular subtype. Positive family history represented 15% of the total population at least one first or second degree relative. Most of the patients were urban habitat accounting for 77% while rural population was only 23%. The median time to begin chemotherapy is 5 weeks (SD= 2.8), ranging from 1-12 weeks. The patients were classified into 4 strata, a total of 36% of patients started chemotherapy in less than 4 weeks, 44.7% waited 4 - 8 weeks, and 14% initiated their chemotherapy within 8 - 12 weeks while only 5% were delayed more than 12 weeks to start their adjuvant chemotherapy. Sociodemographic problems and long residential distance to institution represented the most common cause of chemotherapy delay, while the second cause was system related as late referral and prolonged time needed to get governmental insurance support.

Keywords: Adjuvant Chemotherapy, Non Metastatic Breast Cancer

INTRODUCTION

Breast cancer is the most commonly diagnosed cancer and the leading cause of cancer deaths in women worldwide, accounting for 23% of total cancer cases and 14% of all cancer related mortalities ***(McGuire et al., 2015).***

The lifetime risk of developing breast cancer for women is one eighth. However, >40% of the affected patients are >65 of age account for almost 60% of the total deaths from breast cancer worldwide ***(Siegel et al., 2014).***

In Egypt, breast cancer is the most common type of cancer in females that counts 38.8% of all cancers in females where the age-specific incidence rates show a progressive increase after the age of 30 years, to reach a sharp peak at the age group of 60-64 years ***(Ibrahim et al., 2014).***

The availability of early detection breast cancer screening programs has resulted in increased breast cancer detection rates for all age groups ***(Gotzsche and Nielsen, 2006).***

Female gender is the most important risk factor for breast cancer. Men can develop breast cancer, but the risk for females is about 100 times greater ***(American cancer society, 2014).***

As women advances in age, the risk increases, Caucasian women are slightly more likely to develop breast cancer than

African-American, although African Americans are more likely to die from this disease ***(American Cancer Society, 2014).***

Family history and certain gene mutations strongly increase risk of recurrence. An estimated 5% to 10% of all breast cancers are directly attributable to inherited gene mutations as BRCA1 or BRCA2 genes ***(American cancer Society, 2014).***

Using combined hormone therapy after menopause (estrogen and progesterone) increase risk, also certain reproductive factors as giving birth to a first child after age 30, nulliparity, early menarche and late menopause ***(Chen et al., 2013).***

Early stage breast cancers can be completely resected by Surgery followed by adjuvant treatment and that approach has been the gold standard for breast cancer treatment for a long time ***(Miller et al., 2014).***

Adjuvant treatment modalities improve disease free survival (DFS) and overall survival (OS) in breast cancer patients ***(Bergh et al., 2001).***

Adjuvant treatments for breast cancer can include chemotherapy, hormonal therapy, human epidermal growth factor receptor (HER2)–directed therapies, and radiation ***(Murtuza et al., 2014).***

Chemotherapies are further subdivided into major cytotoxic classes: anti-metabolites, anthracyclines, taxanes, and others, the major endocrine therapies were tamoxifen, aromatase inhibitors, and ovarian suppression (by luteinizing hormone–releasing hormone agonists) or ovarian ablation (by surgery or radiation). For HER2-positive cancers, trastuzumab was the only biologic or targeted agent that was found to have sufficient evidence to be included in the international guideline recommendations ***(Gandhi et al., 2014).***

The proper timing of commencement of adjuvant chemotherapy has been studied for decades, there is in fact a biologic rationale to start chemotherapy as soon as possible after the removal of the primary tumor, however the issue of timing has not received much recent attention from physicians and patients and consequently practice has not changed substantially ***(Senkus et al., 2013).***

This biological rational is supported by ***Gunduz's et al. (1979)*** murine model demonstrating a phase of accelerated growth of residual disease after resection of the primary tumor and the mathematical modeling by ***Goldie et al. (1979)*** demonstrating increasing chemotherapy resistance with time ***(Karen et al., 2014).***

Clinical trials demonstrating that gaining the adjuvant chemotherapy benefit generally require it to be administered