Assessment of Cardiotoxicity in Hormone Positive Postmenopausal Breast Cancer Patients Receiving Aromatase Inhibitors

A Thesis

Submitted For Partial Fulfilment of Master Degree in Clinical Oncology and Nuclear Medicine

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2017

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List of Abbreviations

Abb.	Full term
AI	*Aromatase inhibitors*
AJCC	*American Joint Committee on Cancer*
ALN	*Axillary lymph nodes*
ALNs	*Axillary Lymph Nodes*
APBI	*Accelerated Partial Breast Irradiation*
ASTRO	*American Society for Radiation Oncology*
BCS	*Breast Conservative Surgery*
BMI	*Body Mass Index*
CALGB	*Cancer and Leukemia Group B*
CSR	*Cancer Statistics Review*
DCIS	*Ductal Carcinoma in Situ*
DIBH	*Deep Inspiration Breath-Hold*
E2	*Estradiol*
ER	*Estrogen Receptor*
ET	*Endocraine Therapy*
EUSOMA	*European Society of Breast Cancer Specialists*
FDG-PET	*Fluorodeoxyglucose Positron Emission Tomography*
FNA	*Fine Needle Aspiration*
GnRH	*Gonadotropin-Releasing Hormone*
HBOC	*Hereditary Breast Ovarian Cancer*
HER2	*Human Epidermal Growth Factor Receptor 2*
HR	*Hormone Receptor*
IBTR	*Ipsilateral Breast Tumor Recurrence*
IBTR	*Ipsilateral Breast Tumor Recurrence*
IDC	*infiltrating Ductal Carcinoma*
IHC	*Immunohistochemistry*
ILC	*Infiltrating Lobular Carcinoma*
IMRT	*Intensity-Modulated Radiation Therapy*

List of Abbreviations (Cont...)

Abb.	Full term
ITA	*Italian Tamoxifen Anastrozole*
LAD	*Left Anterior Descending*
LCIS	*Lobular Carcinoma in Situ*
LHRH	*Luteinizing-Hormone-Releasing Hormone*
LV	*Left Ventricular*
M	*Metastasis*
MBC	*Metastatic Breast Cancer*
MLC	*Multi-Leaf Collimator*
N	*Nodal Involvement*
NCRP	*National Cancer Registry Program*
OS	*Overall Survival*
OS	*Overall Survival*
PFS	*Progression-Free Survival*
PFS	*Progression-Free Survival*
PMRT	*Post-Mastectomy Radiation*
PR	*Progesterone*
PR	*Progesterone Receptor*
RS	*Recurrence Score*
SERMs	*Selective Estrogen Receptor Modulators*
SIOG	*Society of Geriatric Oncology*
SLN	*Sentinel Lymph Node*
SREs	*Skeletal-Related Events*
T	*Tumor Size*
TG	*Triglyceride*
TLI	*Thymidine Labeling Index*
WBI	*Whole Breast Irradiation*

ABSTRACT

Major studies shown a significant DFS and OS advantage for different schedules of A.I treatment, including upfront AIs or sequential use of tamoxifen and AIs, have been shown to improve disease-free survival and overall survival compared with tamoxifen alone. The benefit of AIs on breast cancer recurrence and mortality far outweigh the risks of adverse events, and this should be taken into account when considering treatment options for patients. Nevertheless, cardiovascular events reported in clinical trials with AIs raise potential concerns that suggest the need for additional follow-up and studies.

Our cross sectional study that assessed cardiotoxicity for adjuvant and metastatic breast cancer patients at Ain-Shams university clinical oncology department in the interval from August 2016 to June 2017, a total of 123 hormone receptor positive postmenopausal women were treated with Aromatase Inhibitors (AIs) showed evidence of cardiotoxicity by ECHO in 71 patients (57.7% of study population) (P value=0.016). However, it was not detected by blood pressure measurement, lipid profile, ECG. So, ECHO represents an important tool for screening cardiotoxicity that seems to be associated with use of A.I in postmenopausal patients. With the goal of early detection of cancer treatment–related cardiac toxicity, leading to early treatment that results in better survival outcomes.

Keywords: Selective Estrogen Receptor Modulators - Recurrence Score - Post-Mastectomy Radiation

INTRODUCTION

Breast cancer is the leading cause of death among women, and its incidence is increasing with age. The average age at diagnosis is 61 years, and most of deaths occurs beyond the age of 65 years. The best approach to elderly women with breast cancer is still a big challenge. Those patients should have at least a brief general assessment to detect treatable problems, which are not adequately evaluated by the oncologists. The most effective treatment should be provided, unless there are explained reasons against it ***(Tesarova, 2016).***

Breast cancer is considered the second most common cancer overall (1.7 million cases, 11.9%). In females, breast cancer is the most common cancer diagnosed in more and less developed regions, with more cases occurring in less developed (883, 000 cases) than more developed regions (794, 000) ***(Erlay et al., 2012).***

In Egypt, breast cancer is the most common type of cancer which counts for 38.8% of all cancers in women ***(Ibrahim et al., 2014).***

High endogenous estrogen levels increase the risk of breast cancer (particularly hormone receptor-positive) in both premenopausal and postmenopausal women. In postmenopausal women, the correlation between an increased risk for breast

cancer and increased hormone levels (eg: estradiol, estrone) has been fairly consistent ***(Farhat et al., 2011).***

In postmenopausal women, most breast cancers are hormone receptor positive. So, endocrine therapies designed to prevent estrogen driven proliferation, could induce tumor regression ***(Darby et al., 2005).***

Aromatase inhibitors (AI) are used in adjuvant treatment for post-menopausal women with hormone receptor positive breast cancer to reduce the risk of recurrence, and in the metastatic cases to improve overall survival ***(Prince et al., 2016).***

Breast cancer is commonly diagnosed in postmenopausal women who are liable to have 1 or more cardiovascular disease which has a significant competing risk for morbidity and mortality among non-metastatic breast cancer survivors. After treatment completion, adjuvant systemic therapies may result in late-cardiac toxicity after decades. After some adjuvant breast cancer therapies the cumulative incidence of treatment-related cardiotoxic outcomes may be as high as 33%. Treatment–induced cardiotoxicity may manifest as cardiomyopathy, arrhythmias, coronary ischemia, thromboembolism, conduction abnormalities, valvular and pericardial disease ***(Kathryn et al., 2012).***