



Node Negative Breast Cancer In Egyptian Patients At The National Cancer Institute, Cairo University: Correlation With Tumor Size and Molecular Classification.

Protocol of Thesis

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Abstract

Background: Node-negative breast cancer is a prevalent form of the disease worldwide, particularly in regions with rigorous screening and disease awareness efforts. Although there is a common biology between node negative and node positive breast tumors, it is still important to specifically address risk assessment and predictive factors in node negative breast cancer (**Harbeck and Thomssen, 2011**). Different breast cancer subtypes were newly recognized based on immunohistochemistry for ER, PR, HER2/neu and Ki-67, reflecting on patients' prognosis and management. We conducted this study to determine the prevalence of breast cancer subtypes in Egypt (National Cancer Institute, Cairo University) according to immunohistochemistry panel and to explore their association with node negative and other prognostic factors.

Material and Methods: A retrospective study carried out on one hundred and thirteen cases diagnosed as node negative invasive breast carcinoma at the Pathology Department, National Cancer Institute (NCI), Cairo University during the period from January 2007 to December 2010. The cases were classified into luminal A, luminal B, luminal-HER2/neu, HER2/neu-enriched and TNBC, using immunohistochemistry (ER, PR, HER2/neu and Ki-67). The obtained results were correlated with clinico-pathologic variables as well as 5-year DFS and 5-year OS.

Results: Cases were categorized into luminal A (31%), luminal B (35.4%), luminal HER2/neu (9.7%), HER2/neu-enriched (12.4%) and TNBC (11.5%). The majority of cases (85.8%) were low grade while the remaining

cases (14.2%) were high grade. The difference was statistically significant (P value 0.001). Her2-negative cases showed slightly better 5-year DFS than Her2-positive cases with borderline statistical significant difference (89.3% versus 81.7%; respectively) ($p=0.131$). DFS estimates were not significantly different (P 0.975) among different breast subtypes with worst 5-years DFS for TNBC subtype (81.5%). OS estimates were near significantly different (P 0.145) among different breast subtypes whereas TNBC subtype had the worst 5-year OS (49.5%).

Conclusions: TNBC subtype is considered the worst breast cancer subtype. Luminal B is intermediate subtype with variable outcome. Luminal A, luminal HER2/neu and HER2/neu-enriched are expected to behave favorably. OS is expected to be better among hormone-positive versus hormone negative cases. Regarding to HER2 status, HER-2-negative cases achieved better 5-year OS than HER2-positive cases.

By the end of the current study, the conclusion that was achieved is that there wasn't substantial difference in the underlying tumor biology between node-negative and node-positive disease, and the node-negative breast cancer didn't automatically suggest a good prognosis or requiring chemotherapy, and additional biomarkers are needed to help identify those node-negative patients who are expected to behave favorably.

LIST OF CONTENTS

Introduction	1
Aim of work	3
Review of Literature	4
• Breast anatomy and histology	4
• Breast carcinoma	8
➤ Epidemiology	8
➤ Risk factors	10
• WHO classification of epithelial tumors of breast	14
• Invasive carcinoma of no special type, NST	17
• Special subtypes of invasive breast carcinoma	18
• Tumor stage	21
➤ AJCC cancer staging changes from sixth to seventh edition	22
• Prognostic and predictive factors.....	26
• Molecular subtypes of breast carcinoma	30
• Behavior of breast cancer subtypes	35
➤ Significance of ER and PR receptor status	36
➤ ER and PR test scoring	37
➤ ASCO recommendations for ER and PR test	39

• HER2/neu	40
➤ Clinical utility of HER2/neu testing	40
➤ Assessment of HER2/neu status	41
➤ Anti-HER2 Herceptin in Breast Cancer	43
• Ki-67.....	44
➤ The clinical value of ki-67 immunostaining	44
• A new look A New Look at Node-Negative Breast Cancer	46
➤ Node status and relapse rate	47
➤ Risk stratification in node-negative disease	47
➤ Significance of nodal involvement in breast cancer	48
Materials and Methods	50
Results	55
Discussion	79
Summary	89
Conclusions and recommendations	92
References	93
Arabic Summary	115

LIST OF Figures

	<i>Page</i>
Figure (1): Anatomy of the breast (Tezer et al., 2011).....	6
Figure (2): Normal histology of the breast (Visvader, 2009)	7
Figure (3): Estimated Breast Cancer Mortality Worldwide in 2012 (GLOBOCAN 2012 (IARC)	8
Figure (4): Action of Tamoxifen on ER positive breast cancer (Kleinsmith et al., 2010)	37
Figure (5): Diagrammatic description of Allred Score (Choudhury et al., 2010)	38
Figure (6): Herceptin acting on HER2-positive breast cancer cells (Genentech, Inc. 2012)	43
Figure (7): Frequency distribution of studied cases according to gender	55
Figure (8): Frequency distribution of studied cases according to laterality	56
Figure (9): Frequency distribution of studied cases according to location	56
Figure (10): Frequency distribution of studied cases according to tumor type	57
Figure (11): Frequency distribution of studied cases according to tumor size	58
Figure (12): Frequency distribution of tumor grades among the studied cases	58
Figure (13): A case of invasive duct carcinoma, grade I, showing ductal formation > 90% of tumor (hematoxylin and eosin; original magnification X200)	59
Figure (14): A case of invasive duct carcinoma, grade II, showing ductal formation in 10% of tumor and moderate pleomorphism and mitosis 8/10HPF, insit illustrated mitotic figures, (hematoxylin and eosin; original magnification X400)	59
Figure (15): A case of invasive duct carcinoma, grade III with no ductal differentiation, marked pleomorphism and high mitotic activity >20/10HPF, insit illustrated mitotic figures (hematoxylin and eosin; original magnification X400).	60
Figure (16): Frequency distribution of different metastatic sites	61

Figure (17): Frequency distribution of studied cases according to surgical procedure... **62**

Figure (18): Distribution of breast cancer subtypes among studied cases **63**

Figure (19): A case of invasive duct carcinoma, grade II, in a female patient 51 years old, stage T2N0M0, classified as luminal A. (A) Hematoxylin and eosin; original magnification X400. (B) ER: (positive), (C) PR: (positive), (D) HER2/neu: negative, score (0) and (E) Ki-67 LI: 6% (low proliferation index) **64**

Figure (20): A case of invasive duct carcinoma, grade II, in a female patient 59 years old, stage T2N0M0, classified as luminal B. (A) Hematoxylin and eosin; original magnification X400. (B) ER: (positive), (C) PR: (positive), (D) HER2/neu: negative, score (0) and (E) Ki-67 LI: 43% (high proliferation index) **65**

Figure (21): A case of invasive duct carcinoma, grade II, in a female patient 76 years old, stage T2N0M0, classified as luminal HER2/neu. (A) Hematoxylin and eosin; original magnification X400. (B) ER: (positive), (C) PR: (positive) and (D) HER2/neu: positive, score (3) **66**

Figure (22): A case of invasive duct carcinoma, grade II, in a female patient 47 years old, stage T2N0M0, classified as HER2/neu enriched. (A) Hematoxylin and eosin; original magnification X400. (B) ER: (negative), (C) PR: (negative), (D) HER2/neu: positive, score (3) **67**

Figure (23): A case of invasive duct carcinoma, grade II, in a female patient 60 years old, stage T2N0M0, classified as TNBC. (A) Hematoxylin and eosin; original magnification x400. (B) ER: (negative), (C) PR: (negative) and (D) HER2/neu: negative, score (0) **68**

Figure (24): Association between breast cancer subtypes and patient's age **69**

Figure (25): Association between breast cancer subtypes and tumor size (median) **71**

Figure (26): Association between breast cancer subtypes and (T) stage **72**

Figure (27): Association between breast cancer subtypes and anatomic stage **73**

Figure (28): Association between breast cancer subtypes and tumor grade **74**

LIST OF TABLES

	<i>Page</i>
Table (1): TNM staging system of breast cancer, 7 th edition (Edge and Compton., 2010)	24
Table (2): Immunohistochemical Criteria for Defining Breast Cancer Molecular Subtypes (Voduc et al., 2010)	34
Table (3): Systemic treatment recommendations for subtypes (Goldhirsch et al., 2011)	34
Table (4): HER2/neu score used to evaluate Hercept Test (Lester SC, 2006)	42
Table (5): Nottingham combined histologic grade (Ellis et al., 2012)	52
Table (6): The primary antibodies used	53
Table(7): Immunohistochemical Criteria for Defining Breast Cancer Molecular Subtypes, (Cheang et al., 2009)	54
Table (8): Distribution of tumor size among studied cases	57
Table (9): Distribution of tumor anatomic stage among studied cases	60
Table (10): Distribution of hormonal therapy among the observed cases	62
Table (11): Distribution of breast cancer subtypes among studied cases	63
Table (12): between breast cancer subtypes and patients' age	69
Table (13): Association between breast cancer subtypes and site	70
Table (14): Association between breast cancer subtypes and tumor size (median)	71
Table (15): Association between breast cancer subtypes and (T) stage	71
Table (16): Association between breast cancer subtypes and anatomic stage	72
Table (17): Association between breast cancer subtypes and tumor grade	73

Table (18): Disease free survival (DFS) in relation to prognostic factors**76**

Table (19): Overall survival (OS) in relation to prognostic factors **78**

LIST OF ABBREVIATIONS

- **ADH:** Atypical ductal hyperplasia
- **AgNOR:** Argyrophilic nucleolar organizer regions
- **AJCC:** American Joint Committee on Cancer
- **ALH:** Atypical lobular hyperplasia
- **ASCO:** American Society of Clinical Oncology
- **ATM:** Ataxia telangiectasia mutated
- **BC:** breast cancer
- **BCS:** breast conservative surgery
- **BM:** bone marrow.
- **BMI:** body mass index
- **BrdU:** Thymidine labeling index, bromodeoxyuridine
- **CDK:** cyclin-dependent kinase
- **CISH:** Chromogenic in situ hybridization
- **DAB:** 3, 3' diaminobenzinetetrachloride
- **DCIS:** Ductal carcinoma in situ
- **DHEA:** Dehydroepiandrosterone
- **DIN:** Ductal intraepithelial neoplasia
- **DFS:** Disease free survival

- **EGFR:** epidermal growth factor receptor
- **ELISA:** enzyme-linked immunosorbent assay
- **ER:** Estrogen receptor
- **ERK:** Extracellular-signal regulated kinase
- **ETD:** extralobular terminal duct
- **FISH:** Fluorescence in situ hybridization
- **HER2:** The human epidermal growth factor receptor 2 gene
- **HER/ErbB:** human epidermal growth factor
- **HT:** Hormonal therapy
- **H & E:** hematoxylin and eosin staining
- **IARC:** International Agency for Research and Cancer
- **IDC:** invasive ductal carcinoma
- **IHC:** immunohistochemistry
- **IM:** internal mammary node
- **ITD:** intralobular terminal duct
- **(i+):** +ve by IHC
- **Ki-67 LI:** Ki-67 labeling index
- **LBD:** ligand binding domain
- **LCIS:** Lobular carcinoma in situ
- **LIN:** Lobular intraepithelial neoplasia

- **LFS:** Li-Fraumeni syndrome
- **LN:** lymph node
- **LR:** local recurrence
- **M:** distant metastases
- **MAP kinase:** mitogen activated protein kinase
- **MoAbs:** Monoclonal antibodies
- **MRI:** Magnetic resonance imaging
- **N:** regional lymph nodes
- **NBF:** Neutral buffered formalin
- **NCCN:** National Comprehensive Cancer Network
- **NCI:** National Cancer Institute
- **NGS:** Nottingham Grading System
- **NOS:** not otherwise specified
- **NST:** no special type
- **PAI-1:** plasminogen activator inhibitor-1
- **PARP inhibitors:** Poly(ADP-Ribose)polymerase inhibitors
- **PCB's:** polychlorinated biphenyls
- **PCR:** polymerase chain reaction
- **pCR:** pathologic complete response
- **PJS:** Peutz-Jeghers syndrome

- **PKB** : Protein Kinase B
- **PR**: Progesterone receptor
- **PTEN**: phosphatase and tensin homolog
- **RT-PCR**: reverse transcriptase polymerization chain reaction
- **RR**: regional relapse
- **SEER**: Surveillance, Epidemiology, and End Results
- **SISH**: Silver-enhanced in situ hybridization
- **T**: primary tumor
- **TDLU**: Terminal duct-lobular unit
- **TGFβ**: transforming growth factor beta
- **Tis**: Carcinoma in situ
- **Tis (DCIS)**: Ductal carcinoma in situ.
- **Tis (LCIS)**: Lobular carcinoma in situ.
- **TNBC**: triple-negative breast cancer
- **Tis (Paget's)**: Paget's disease of the nipple NOT associated with invasive carcinoma and/or carcinoma in situ (DCIS and/or LCIS) in the underlying breast parenchyma.
- **UICC**: International Union for Cancer Control
- **Upa**: urokinase plasminogen activator
- **WHI**: Women's Health Initiative