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Impact of molecular subtypes classification concordance between preoperative core needle biopsy and surgical specimen on early breast cancer management: Single-institution experience and review of published literature

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Abstract

Background: Core needle biopsy (CNB) plays a crucial role as diagnostic tool for breast cancer (BC). The characterization of biomarkers status before surgical treatment is crucial when primary systemic therapy is a therapeutic option. The aim of this analysis was to report concordance between preoperative CNB and surgical specimen (SS) in evaluating biomarkers and molecular subtypes.

Methods: Data have been collected from a cohort of 101 patients affected by early BC treated at Careggi Florence University Hospital, between January 2014 and March 2015. The conformity between molecular subtype classification was tested using kappa (κ) test.

Results: Mean age was 57.5 years (range 29–86). There was concordance between the estrogen receptor (ER) assessment on CNB and SS in 95 cases (94.1%). Concordance of the progesterone receptor (PgR) assessment was observed in 89 cases (88.1%). Concordance for detecting immunohistochemistry-assessed BC molecular subtypes was 87.1% ($\kappa = 0.78$). Concerning Ki-67 evaluation, we report a concordance rate of 88.1% ($\kappa = 0.68$). The evaluation of luminal A plus luminal B/HER negative subgroup showed a κ-value of 0.65.

Conclusions: CNB showed good accuracy in evaluating hormonal receptors status, HER2, and BC molecular subtypes. Evaluation of Ki67 status was less accurate than other biomarkers; therefore, we recommend that it should be detected both on CNB and SS samples, especially in hormonal positive HER2 negative tumors, in order to avoid a misclassification of tumor subtypes that could lead to an omission of potential effective systemic therapy.

Keywords: Breast cancer; Core needle biopsy; Ki-67 proliferative index; Estrogen receptor; Surgical specimen; Molecular subtypes

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Introduction

Breast cancer (BC) represents the second most common cancer (11.9% of solid tumors) and the most frequent cancer among women (25%), with a progressive increasing incidence.[1,2] BC incidence widely differs across the world areas from 27 per 1,00,000 in Middle Africa to 96 in Western Europe. The age-standardized incidence rate per 1,00,000 has globally increased by 17% in recent years (46% in developing countries, and 8% in developed countries).[2,3]

Nowadays, biomarkers such as estrogen receptor (ER), progesterone receptor (PgR), human epidermal growth receptor factor 2 (HER2) and Ki-67 proliferative index assessment represents the key-point to tailor BC treatment. Biomarkers are strong predictive factors for response to treatments and long-term prognosis. Moreover, HER2 over-expression is a possible marker of resistance to certain endocrine and chemotherapy treatments.[4,5]

BC has to be considered a heterogeneous disease; several molecular analyses (i.e. microarray) identified four subtypes of BC, including Luminal A, Luminal B, HER2 enriched, and triple negative cancers. The oncology community recommends to consider these subtypes in order to classify and guide BC management, using immunohistochemistry (IHC) data as surrogates.[6–8]

Core needle biopsy (CNB) has become a crucial diagnostic tool for BC, and it is considered the gold standard for tissue sampling for breast lumps.[9] The characterization of biomarkers status before surgical treatment is crucial when primary systemic therapy is a therapeutic option. Moreover, CNB seems to be characterized by optimal fixations conditions when compared to surgical specimens (SS) slicing and fixing protocols.

Few studies have evaluated the agreement between biomarkers status evaluated on CNB and the subsequent SS, with results widely differ, ranging between 79% and 100%.

These contradictory results are thought to be related to the non-homogeneous distribution of the antigens within the tumors[10–17]; therefore, the debate if BC necessitates further IHC staining on SS is still open.

The purpose of this paper was to report our single-center experience on concordance between the CNB and the SS in evaluating biomarkers and molecular subtypes of early BC.

Patients and methods

Patients

From January 2014 to March 2015 we retrospectively collected data from patients affected by early BC presenting to the Diagnostic Senology Unit of the Careggi Florence University Hospital. All patients underwent CNB and subsequent surgical excision (SE). The local institutional review board (IRB) approved this retrospective analysis and a written informed consent was not required.

The inclusion criteria for the study were histological diagnosis of BC on 14 Gauge (14-G) CNB, and available complete histological reports of CNB and SS. Patients who received primary chemotherapy were excluded, due to significant influence on the postoperative expression of biomarkers.[18]

Radiology methods

Percutaneous CNB were performed under local anesthesia with a semi-automated biopsy gun (Precisa, Hospital Service; Rome, Italy) with a 14-G, 10 cm long needle. A mean of 3 core samples per lesion (range 3–7) were obtained. In all cases an ultrasound guidance was utilized, as all lesions were visible on sonography.

The database of the local institution was consulted to categorize both the histological diagnosis and biomarkers on CNB and on SS. Definitive histological diagnosis and biomarkers on SS served as the gold standard in the treatments decision-making process.

Pathology methods

ER status, PgR status, and Ki-67 labeling index determined with the Mib-1 monoclonal antibody were evaluated on every specimen. For ER and PgR status two categories (negative/positive) were considered according to predetermined cut-off values (10% for both ER and PgR) based on values commonly used in the scientific community.[19] HER2 status assessed by IHC using HercepTest® (Dako) was categorized as follows: 0, no staining or weak membrane staining in less than 10% of tumor cells; 1+, weak membrane staining in more than 10% of tumor cells, incomplete membrane staining; 2+, weak to moderate membrane staining in more than 10% of tumor cells; and 3+, intense circumferential membrane staining in more than 10% of tumor cells. HER2 scores of 0 and 1+ were categorized as HER2 negative. All IHC 2+ tumors were subsequently tested for gene amplification by fluorescent in situ hybridization (FISH). Tumors were considered HER2 positive in case of IHC score 3+ or positive FISH test. Histological tumor grading was evaluated according to Elston and Ellis.[20]

We categorized BC tumors as Ki-67 high or low using a non-inclusive 15% of cut-off value, although the ideal threshold it is still a matter of debate, and proposed cut-off values vary widely from 1 to 28.6%.[21] Ki-67 was assessed as an estimation at high power field exclusively including hot spots.

Concerning the evaluation of ER and PgR by IHC the following validated primary antibodies were applied[22]: anti-ER, clone 6F11 (Ventana Medical Systems, Tucson, Arizona); anti-PgR: clone 16 (Ventana Medical Systems, Tucson, Arizona); anti-Her2/neu: policlonal A0485 (DAKO, Denmark); anti-Ki-67: clone Mib-1 (Immunotech, Marseille, France). The following categories were adopted

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