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Editorial

Breast Cancer; Molecular Subtyping and Surgical Decision

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Editorial

It is always observed that patients with breast cancer tumors with similar clinical and pathological presentations may have different behaviors. It is generally recognized that disease of the same stage behaves differently. The biologic reasons for recurrence and resistance of breast cancer to treatment are poorly understood. The standard prognostic factors namely; histologic subtype, margin status, axillary nodal status, tumor grade, age and comorbidities are not suffuicient as an explanation. The histological appearance of the tumors by simply defining them as ductal or lobular may not be sufficient to establish the underlying complex genetic alterations and the biological events involved in cancer development and progression. Perou et al. (nature 2000) first analyzed gene expression patterns in grossly dissected normal or malignant human breast tissues. They identified a number of clearly different molecular phenotypes observed among the breast tumours [1]. Since then, breast cancer is looked at as a heterogeneous complex of diseases and a spectrum of many subtypes with distinct biological features that lead to differences in response patterns to various treatment modalities and clinical outcomes. Five biological breast subtypes are identified namely: luminal A, Luminal B, Her 2 enriched, Basal like & triple negative non basal. On this basis, one might consider these molecular subtypes as separable diseases. They provide prognostic information that may facilitate treatment decisions and differences in survival. However, data is lacking about their impact on loco-regional recurrence which is very much related to the adequacy of surgical treatment. So the question is should we tailor the surgical intervention based on the subtype to reduce loco-regional recurrence? To date, relatively few studies have attempted to find an association between breast cancer molecular subtype and loco-regional recurrence. Luminal A tumors had the most favorable prognosis while HER2-enriched and basal-like groups showed highest rate of local & regional recurrence (approximately 20% *vs.* 8% for luminal A). The loco-regional relapse patterns observed among the various breast cancer subtypes were similar whether the patients are treated with breast conservative surgery or mastectomy. There is insufficient evidence to suggest that breast conservation is inappropriate for non-luminal type breast cancer [2].

It is a well known fact that negative margins achieve the lowest risk of recurrence when compared to positive margins if breast conservative surgery is selected as a surgical option for the patient. No ink on the tumor is sufficient and agreed upon as a guideline for excising malignant breast tumors. Does this act applies to the different pathological subtypes and, should the margin width be increased when breast conservative surgery is selected high risk subtypes to guard against tumor recurrence? A meta-analysis of 33 studies comprising 28162 patients undergoing breast conservative surgery and reporting on surgical margins and local recurrence found that margin width is not a predictor of local recurrence [3]. In a study conducted on triple negative breast cancer undergoing breast conservative resection compared; excision of the tumor with a safety margins more than and less than 2mm width found no significant impact difference on local recurrence [4]. In addition, local control has been attributed to the introduction of the new targeted therapy regardless the type of surgery applied [5,6].

Thus, as a conclusion surgical intervention should not be tailored based on the subtype because surgery does not trump biology.

Since the application of Sentinel Lymph Node (SLN) concept, it has been realized that there is no difference in the overall survival, disease-free survival, and regional control in node negative patients if SLN is applied compared with axillary dissection. SLN alone is safe and effective in these patients (NSABP B-32 trial) [7]. Moreover, the ACOSOG Z-0011 trial recommended no need for nodal dissection in T1-2 cN0 if ≤ 2 SL nodes are positive [8]. Does this apply in the management of the axilla in high risk tumors like triple negative and Her 2 enriched subtypes i.e is sentinel biopsy only sufficient for N0?. and are they candidates for ACOSG Z0011 trial. Lymphovascular Invasion (LVI) is a well known marker for metastatic potential of the tumor. The risk for LVI in other biological breast cancer subtypes was found statistically higher than in Triple Negative Breast Cancer (TNBC). It seems that TNBC spread via lymphatics less frequently than other subtypes and axillary lymph node dissection may be avoided in TNBC patients meeting Z0011 eligibility criteria [9]. Thus, the proper selection breast cancer subtypes may be an important factor determining the need for axillary lymph node dissection in patients with luminal breast cancer subtypes, and dissection may not be necessary in some TNBC patients depending of the result of the examined SLN. In addition, in the high risk biological breast cancer subtypes the sentinel lymph node is sufficient in assessment of axillary lymph node status in No tumors and there is no need to do axillary dissection if the <2 positive sentinel lymph nodes are detected. This is explained by the fact that the high risk types have the lowest risk of non sentinel lymph node metastases in breast cancer patients with positive sentinel lymph node [10].

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