



THE IMPACT OF AGE ON LOCAL RECURRENCE IN EARLY STAGE BREAST CANCER

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Breast cancer is a systemic malignant disease with many facets. Because micro-metastasis can be found during the early stages of this disease is very important to start treatments including surgery, chemotherapy, hormonal therapy, radiotherapy, immunotherapy in early stage of the disease. Now, breast-conserving therapy has become a standard treatment for stage I and stage II breast cancer. For individual treatment decisions, it is important to appreciate the heterogeneity of disease. In the treatment of the disease we must take into account the factors that are related to the molecular biology of the tumour and to the patient-related factors. One of the most important of patient-related factors is the age of the patient at diagnosis.

Keywords: breast, conserving therapy, recurrence, histology, early stages.

INTRODUCTION

Breast cancer is the most common type of cancer in women (24.2%) with an estimated number of more than 2 million new cases worldwide in 2018¹. According to the Globocan, breast cancer is the leading global cause of cancer-related death among women (15%) with approximately 627,000 breast cancer-related deaths in 2018¹. Micro-metastasis can be found in the early stage of the disease and it is very important to choose the best method of treatment. Modified radical mastectomy was first performed in the 1970s and now for stage I and stage II, breast-conserving therapy has become a standard treatment. According to accumulated data from prospective clinical studies on breast-conserving therapy, the consensus among experts is that there are no significant differences in the local recurrence and mortality rates between conserving therapy and radical mastectomy in breast cancer patients^{2,3}. There are two types of local recurrence post breast conserving therapy: true recurrence and new primary tumours.

DEFINITION OF LOCAL RECURRENCE

Unfortunately there is no consistent definition for local recurrence used in the literature, making

comparison of studies somewhat challenging. Depending on the publication, local recurrence has included nodal recurrence, skin recurrence, all recurrences in the ipsilateral breast or selective ipsilateral breast recurrences. Given that the difference between mastectomy and breast conserving surgery is the extent of surgery in the breast, most authors have not included auxiliary nodal recurrence in their definition of local recurrence. There is no evidence that could be found to support the concept that nodal recurrence is increased in breast conserving surgery supporting the majority of authors who have not included it in their definition. A recurrence of malignancy in the ipsilateral breast could, in theory, be due to recurrence of residual disease or a new primary malignancy, a concept first articulated by Veronesi⁴. The literature addressing this question suggests that there is likely a difference in the biological significance of these two theoretical events and an attempt to distinguish between them would be reasonable for that reason alone⁴⁻⁷. According to the hypothesis advanced by Veronesi, true recurrences are cases consistent with re-growth of malignant cells not removed by surgery and not killed by adjuvant radiotherapy. New primary tumours however are new malignancies arising from residual breast epithelium. Subsequent literature suggests that this concept is likely true with new primary malignancies having a better prognosis than true

recurrences. While both types of recurrence are a consideration with breast conserving therapy only true recurrences would be affected by the extent of resection of the primary tumour assuming that the incidence of new primary tumours is the same whether the person had a small amount of breast tissue removed or a larger one. Komoike *et al.* used location of the primary and secondary tumour, initial surgical resection margin and other pathology to distinguish true recurrences from new primaries while others used location histology and DNA flow cytometry or just location and histology.⁸ Abd-Alla *et al.* provides us with a useful clinical definition in which an ipsilateral breast recurrence was considered a true recurrence if it was located within 3 cm of the primary tumour bed and had a histological subtype consistent with the primary tumour⁵. While the current methods described to differentiate a true recurrence from a new primary tumour are useful when the local recurrence is in a separate quadrant of the breast or of a different histology tumour heterogeneity makes it extremely difficult to distinguish the two when the local recurrence occurs in the same general location in the breast as the primary malignancy and is of the same histology. It is likely that genetic markers will aid in distinguishing true recurrence from new primaries in the future.

AGE AS A VARIABLE ASSOCIATION WITH RECURRENCE

Young age is the most consistently found variable to be associated with local recurrence in breast conserving therapy^{9, 10-17}. Exactly what age is used to define "young" varies from 32 to 50 with the vast majority of authors using age 35 or 40 as the cut off. Not only is this variable the most consistently found association with local recurrence it is the strongest association next to radiation therapy. Having said that one study looking specifically at the question of age found no association¹⁸. They found instead that other factors, such as positive margin, high grade, extensive duct carcinoma in situ and lympho-vascular invasion predicted for local recurrence better. In fact, in their multiple variable regression model age was not an independent predictor at all. Moreover, many of the articles that used multiple variable regression did not find age to be an independent predictive variable^{19,20}.

CONCLUSIONS

This year in St.Gallen Consensus Conference was discussed treatment recommendations and treatment optimization for early breast cancer. For stage I and stage II young women, breast conserving therapy has become a standard treatment. Hypo-fractionated breast irradiation can be used for most patients as a care standard for all patients, not only following breast conservation. Many of the articles that used multiple variable regression did not find age to be an independent predictive variable, it found that other factors like lympho-vascular invasion, high grade are predicted for local recurrence.

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