

Omission of Radiation Therapy (RT) for Metaplastic Breast Cancer (MBC): A Review Article

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ABSTRACT

Background: Metaplastic breast c ancer (MBC) is a unique pathological entity characterized by histologic presence of 2 or more cellular types frequently representing mixed epithelial and mesenchymal components. Although comprising a small proportion of all breast cancers, MBC may have a distinct clinical behavior typically with an aggressive disease course in affected patients. Optimal therapeutic strategies for management of MBC have yet to be defined. Extrapolation of evidence for management of frequent types of breast cancer such as invasive ductal carcinoma has been considered, however, MBC may require thorough and more intensive management with its distinctive features given the poorer prognosis and aggressive disease course. Radiation therapy (RT) has a critical role in management of breast cancer with several studies addressing its utility for achieving improved therapeutic outcomes. However, adverse effects of irradiation has been an important concern with improved survival of patients due to more effective therapies. Radiation induced toxicity such as pneumonitis, cardiac morbidities, secondary cancers along with impaired cosmesis may lead to severe consequences although modernized RT techniques and equipment hold promise. Quality of life has been a critical aspect of contemporary management strategies, and sparing of selected patients from adverse effects of irradiation has been considered. Omission of postoperative RT for selected early stage breast cancer patients has been suggested in several studies, however, there is paucity of data on patients with MBC.

Materials and Methods: Herein, we provide a concise review of RT omission in MBC.

Results: There is not adequate high quality evidence to support RT omission for MBC.

Conclusion: Given the typically poorer prognosis of MBC with an aggressive clinical course in a considerable proportion of affected patients, being more conservative for omission of RT may be considered even in elderly patients with earlier stages of disease.

Keywords: metaplastic breast carcinoma (MBC), omission, radiation therapy (RT)

INTRODUCTION

Metaplastic breast cancer (MBC) is a unique pathological entity characterized by histologic presence of 2 or more cellular types frequently representing mixed epithelial and mesenchymal components, and although comprising a small proportion of all breast cancers, MBC may have a distinct clinical behavior typically with an aggressive disease course in affected patients [1-9]. Optimal therapeutic strategies for management of MBC have yet to be defined. Extrapolation of evidence for management of frequent types of breast cancer such as invasive ductal carcinoma has been considered, however, MBC may require thorough and more intensive management with its distinctive features given the poorer prognosis and aggressive disease course. Specifical features of MBC may include larger tumor size, triple negative disease, and higher expression of Ki-67 and EGFR [1,6,8,10-12].

Radiation therapy (RT) has a critical role in management of breast cancer with several studies addressing its utility for achieving improved therapeutic outcomes [13-16]. However, adverse effects of irradiation has been an important concern with improved survival of patients due to more effective therapies. Radiation induced toxicity such as pneumonitis, cardiac morbidities, secondary cancers along with impaired cosmesis may lead to severe consequences although modernized RT techniques and equipment hold promise. Quality of life has been a critical aspect of contemporary management strategies, and sparing of selected patients from adverse effects of irradiation has been considered. Omission of postoperative RT for selected early stage breast cancer patients has been suggested in several studies, however, there is paucity of data on patients with MBC [17-19].Herein, we provide a concise review of RT omission in MBC.

OMISSION OF RT IN MBC

Omission of RT for selected patients with early breast cancer has been considered in view of important studies addressing this issue [17-19]. Fyles et al. studied on patients ≥ 50 years old and assigned them to receive tamoxifen alone versus tamoxifen plus breast RT [17]. Median follow-up duration was 5.6 years, and patients not receiving RT had higher local relapse rates at 5 years [17]. Distant relapse, overall survival, and breast cancer death results were not significantly different between the groups [17]. It is important to note that large tumors up to 5 centimeter were included in the study without the requirement of hormon receptor positivity [17]. Nevertheless, subgroup analysis including estrogen receptor positive tumors ≤ 2 cm has also revealed that local recurrence rate was3.6% versus 15.2% suggesting a critical role for RT in reducing local recurrences [17].

CALGB 9343 study has included patients over 70 years of age with clinical stage I, estrogen receptor positive breast cancer [18]. Patients were randomly assigned to receive tamoxifen plus irradiation versus tamoxifen alone after lumpectomy [18]. Median follow-up duration of 12.6 years for treated patients, and rates of freedom from local and regional recurrences was 98% versus 90% for patients receiving tamoxifen plus irradiation and tamoxifen alone, respectively [18]. Time to mastectomy, time to distant metastasis, breast cancer specific survival, and overall survival results were not significantly different between the 2 groups [18].

PRIME II randomized controlled trial included patients over 65 years of age with low risk features including hormone receptor positivity, axillary node negativity, T1-T2 tumors up to 3 cm at largest dimension, and clear margins [19]. At a median follow-up duration of 5 years, ipsilateral breast tumor recurrence was 1.3% and 4.1% for patints receiving and not receiving RT, respectively [19]. Again, overall survival, regional recurrence, distant metastases, and new breast cancers were not significantly different between the 2 groups [19].

While these studies typically included patients with common breast cancer subtypes, omission of RT for MBC has been poorly addressed in the literature. Haque et al. assessed omission of RT in elderly patients with early stage MBC [20]. All patients were ≥ 70 years of age and had T1 or T2, lymph node negative disease [20]. Omission of RT steadily declined over the study period and RT delivery was found to be less likely in the setting of not receiving hormone herapyor age≥ 80 years [20]. Multivariate analysis revealed that advanced age, higher T stage, high grade disease and omission of RT was independently associated with poorer overall survival [20]. Given the independent association with worse survival, the study did not support routine omission of RT for these patients [20].

CONCLUSIONS AND FUTURE PERSPECTIVES

Given the typically poorer prognosis of MBC with an aggressive clinical course in a considerable proportion of affected patients, being more conservative for omission of RT may be considered even in elderly patients with earlier stages of disease.

Radiation oncology discipline has undergone unprecedented advances in recent years with adoption of adaptive irradiation strategies, contemporary technologies, along with contemporary treatment delivery techniques such as incorporation of molecular imaging, automatic segmentation methods, Intensity Modulated RadiationT herapy (IMRT), Image Guided Radiation Therapy (IGRT), Adaptive Radiation Therapy (ART), Breathing Adapted Radiation Therapy (BART), and stereotactic irradiation [21-76].

In the context of RT omission for MBC, there is not adequate high quality evidence to support this strategy. Clearly future studies are required to shed light on this issue.

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Citation: Omer Sager et al., "Omission of Radiation Therapy (RT) for Metaplastic Breast Cancer (MBC): A Review Article", International Journal of Research Studies in Medical and Health Sciences. 2021; 6(1): 10-15. DOI: https://doi.org/10.22259/ijrsmhs.0601002

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