

# Global Research in Gynecology and Obstetrics

## Review Article

### Neoadjuvant or Adjuvant Systemic Treatment for Early Breast Cancer: A Radiation Oncology Perspective

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#### Abstract

**Background:** Optimal management of breast cancer patients warrants thorough multidisciplinary and individualized assessment by surgical oncology, medical oncology, and radiation oncology. Chemotherapy, which constitutes a major component of multimodality breast cancer management, may be used in the neoadjuvant or adjuvant setting with promising outcomes. Utility of neoadjuvant or adjuvant chemotherapy in multimodality management of early breast cancer has been debated and is currently an area of active investigation.

**Materials and Methods:** We provide a concise review of neoadjuvant versus adjuvant chemotherapy for early breast cancer from a radiation oncology perspective in light of the literature with focus on recent studies and high quality evidence.

**Results:** In the context of systemic management of breast cancer, an important focus in research is about sequencing of chemotherapy as neoadjuvant or adjuvant treatment. Neoadjuvant chemotherapy approach may provide tumor downsizing and consequent reduction in extent of surgery. Recent concepts also include its utilization for operable breast cancer patients with accumulating data in support of this strategy.

**Conclusion:** Several strategies are being investigated to improve the therapeutic ratio for patients suffering from breast cancer. Response to neoadjuvant chemotherapy may have several implications for prognosis and decision making. While

neoadjuvant therapy was primarily utilized for management of inoperable breast cancers previously, its use has expanded with growing body of evidence from recent studies. Clearly, future studies are warranted to assess neoadjuvant and adjuvant chemotherapy for early breast cancer management.

**Key words:** Breast cancer, Chemotherapy, Neoadjuvant, Adjuvant

## Introduction

Breast cancer is among the most frequent cancers and a leading cause of cancer related deaths in women [1-3]. Nevertheless, breast cancer detection in earlier stages has substantially increased recently owing to enhanced public awareness along with contemporary screening and imaging strategies. In addition, institution of modern therapy approaches and advances in multimodality management with surgery, radiation therapy (RT), and systemic treatment may translate into great achievements in overall outcomes of management. In this context, life expectancies of patients with early stage breast cancers have improved with more effective treatments. Consequently, increased survival rates in breast cancer patients rendered quality of life an endpoint of utmost importance. RT has a major role in multimodality management of breast cancer, nonetheless, toxicity associated with irradiation such as impaired cosmesis, radiation pneumonitis, cardiac toxicities, and secondary cancers may comprise significant concerns with great potential to cause quality of life deterioration in affected patients. Randomized trials provide high level evidence regarding the utility of irradiation in the postmastectomy setting following breast conserving surgery [4-6]. Tumor size  $\geq 5$  centimeters, involved margins, and  $\geq 4$  positive axillary nodes have been traditionally considered as high risk features which could indicate increased benefit of irradiation in the postmastectomy setting. Current recommendations support the use of RT after breast conserving surgery in patients with early breast cancer in the context of achieving improved local control rates.

Neoadjuvant chemotherapy for breast cancer may be described as the use of systemic therapy before surgical resection. This approach has potential for converting inoperable breast tumors into operable tumors which may improve treatment outcomes. Adjuvant chemotherapy refers to administration of systemic therapy following surgery for breast cancer management particularly for decreasing the risk of distant metastases. Utility of neoadjuvant

or adjuvant chemotherapy in multimodality management of early breast cancer is an area of active investigation. Within this context, we provide a concise review of neoadjuvant versus adjuvant chemotherapy for early breast cancer from a radiation oncology perspective in light of the literature with focus on recent studies and high quality evidence.

## Neoadjuvant versus Adjuvant Chemotherapy for Early Breast Cancer

Breast cancer is a major health concern due to its high prevalence and mortality in women [1-3]. State of the art imaging techniques, improved screening capabilities and increased public awareness has led to detection of breast cancer in earlier stages in the millennium era. Optimal management of breast cancer patients warrants thorough multidisciplinary and individualized assessment by collaborative effort of experts from surgical oncology, medical oncology, and radiation oncology. Critical factors considered in decision making for management may include age, disease stage, tumor size, nodal involvement status, patient preferences, and logistical issues. Irradiation after mastectomy or breast conserving surgery may improve treatment results as suggested by landmark trials addressing this issue [4-6].

Chemotherapy, which constitutes another major component of multimodality breast cancer management, may be used in the neoadjuvant or adjuvant setting with promising outcomes. Utility of neoadjuvant or adjuvant chemotherapy in multimodality management of early breast cancer has been debated and is currently an area of active investigation.

A recent meta analysis of individual patient data from 10 randomized trials has addressed long term outcomes for neoadjuvant versus adjuvant chemotherapy in early breast cancer [7]. In the metaanalysis, thorough assessment was performed regarding neoadjuvant chemotherapy and the same chemotherapy delivered post-operatively. Effects of patient and tumor characteristics on

tumor response, extent of local treatment, local and distant recurrences, breast cancer mortality, and overall mortality were evaluated comprehensively. A total of 10 trials including 4756 patients were assessed, and clinical response and breast conserving therapy rates were found to be higher in smaller, higher grade, and hormone receptor negative tumors. Though responders to neoadjuvant chemotherapy suffered from lower distant recurrences and breast cancer death compared to non-responders, when responders and non-responders were combined, distant recurrences and breast cancer death were comparable with neoadjuvant and adjuvant chemotherapy. Nonetheless, local recurrence was found to be higher with neoadjuvant chemotherapy compared to adjuvant chemotherapy, which persisted for 10 years posttherapy. Downsizing of tumors with neoadjuvant chemotherapy may allow for increased rates of breast conserving therapy, and this strategy may also provide data on response to a particular chemotherapy regimen individually. However, no superiority of neoadjuvant chemotherapy exists in the context of reducing breast cancer death. Moreover, neoadjuvant chemotherapy was found to be associated with moderately increased risk of local recurrences persisting for at least 10 years, which may partly be explained with the reduction of the extent of surgery [7].

A comprehensive review by Montemurro et al. addressed the debate on neoadjuvant versus adjuvant chemotherapy for early breast cancer management [8]. The authors emphasized that the delivery of systemic treatment before surgery has evolved from a contingency in inoperable patients to a viable therapeutic option for operable breast cancer. Potential benefits of neoadjuvant chemotherapy were addressed as downstaging of tumors and allowing for less extensive surgery. It has been mentioned that failure of neoadjuvant chemotherapy in eradication of disease from breast and axilla could portend a poorer prognosis particularly in the setting of triple negative or human epidermal growth factor receptor 2 (HER2) positive disease. Outcomes of recent data from randomized trials were addressed, and demonstration of benefit with delivery of systemic agents in the postsurgical period in the setting of persistent disease after neoadjuvant chemotherapy for triple negative or HER2 positive breast cancer was suggested as a potential basis for promising further research. The authors concluded that neoadjuvant chemotherapy could serve as a preferred

therapeutic strategy for triple negative or HER2 positive breast cancer in view of encouraging outcomes from recent results consolidating the role of complete pathological remission as a critical treatment endpoint and guide for decision making [8].

Clearly, the issue of neoadjuvant or adjuvant chemotherapy for early breast cancer management should be thoroughly assessed in future studies to shed light on considerations in individualized treatment strategies.

## Conclusions and Future Perspectives

Breast cancer is a prevalent condition and accounts for a considerable proportion of procedures (or similar word) in major cancer centers. Earlier detection is being increasingly common with advances in screening, imaging methods, and public awareness. Several strategies are being investigated to improve the therapeutic ratio for patients suffering from breast cancer.

In the context of systemic management, an important focus in research is about sequencing of chemotherapy as neoadjuvant or adjuvant treatment. Neoadjuvant chemotherapy approach may provide tumor downsizing and consequent reduction in extent of surgery. Also, response to neoadjuvant chemotherapy may have several implications for prognosis and decision making. While neoadjuvant therapy was primarily utilized for management of inoperable breast cancers previously, its use has expanded with growing body of evidence from recent studies. Clearly, future studies are warranted to assess neoadjuvant and adjuvant chemotherapy for early breast cancer management.

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