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REVIEW

# Breast conservation in locally advanced breast cancer in developing countries: Wise or waste

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**Abstract**
Breast conservation as an additional benefit was beyond the initial expectations of the investigators who pioneered neoadjuvant chemotherapy (NACT). In recent years an increasing number of patients with locally advanced breast cancer (LABC) are being treated with NACT, followed by breast conservation surgery with axillary dissection and radiation as a part of the multimodality management. Breast conservation has not been the standard of care for women with LABC, owing to concerns of increased chances of local recurrence, and possible survival disadvantage and psychological trauma from experiencing a recurrence of malignancy.

LABC is still a common form of presentation of breast cancer in developing countries. Strict adherence to treatment protocols and regular follow-ups for years may not be practical for a large majority of patients hailing from the regions most affected by LABC. Defaulters often thus have a heavy price to pay.

Hence lies the importance of carefully selecting LABC patients for a breast conservation approach from others that would have a higher risk of locoregional recurrence. Can we extrapolate the lessons learnt in early breast cancer to LABC and offer selected patients with LABC breast conservation therapy? Would the local control and survival results with conservative therapy be comparable to those obtained using mastectomy, or does the increased tumor burden in LABC necessitate ablative surgery in all women? This review aims to address these important questions.


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**Contents**



## Neoadjuvant chemotherapy in locally advanced breast cancer

Locally advanced breast cancer (LABC) represents a heterogeneous group of tumors ranging from slow growing neoplasms to rapidly proliferating and aggressive ones. Patients with these cancers include those with operable disease at presentation (American Joint Committee on Cancer (AJCC) clinical TNM (Tumor Node Metastasis) stage T3N0, T3N1M0), inoperable disease at presentation (AJCC clinical stage IIIA (except T3N1M0), IIIB or IIIC) that includes inflammatory breast cancer (AJCC clinical stage T4d, Any N, M0) [1]. LABC represents only 2—5% of all breast cancers in the United States compared to 50—70% in India [2,3]. Despite this fact only very few studies from the developing nations have published their data on breast conservation in LABC. Thus most of the current understanding on the said subject is derived from single institution's experience and trials conducted across the world.

Since its initial use in the early 1970s, neoadjuvant chemotherapy (NACT) has become the standard of care for management of LABC and is increasingly being used for treatment of early-stage breast cancer [4]. It is presumed to have several advantages such as it can downsize large tumors, thus allowing breast conserving surgery in patients' so desiring, it provides in vivo information on tumor response to a specific chemotherapeutic agent, and probably helps in achieving longer disease-free survival (DFS) and overall survival (OS) [5]. In general, majority of patients achieve clinical response rates (60—90%) to NACT [6]. Complete pathologic remissions are however noted in only 3—30% of patients in most trials [7]. Although a few patients experience mixed responses (response in the primary tumor and no response in the lymph nodes and vice versa) for most patients' response is similar in all sites of tumor involvement. Pathological complete responses (pCR), now defined as no invasive or noninvasive tumor in the breast and axillary tissues removed at time of surgery, seem to be the most powerful predictor of outcome in terms of survival [8,9]. However, it should be remembered that patients with pathologic complete response can still experience disease recurrence. Results from several clinical trials reveal that pathologic positive node status after NACT is strongly associated with inferior OS and DFS compared with negative node status [10—13].

## Evolution of the concept of breast conservation following neoadjuvant chemotherapy

Encouraged by the success of NACT in downstaging large breast tumors, efforts were directed to find out if NACT was in any way better than adjuvant chemotherapy in terms of DFS and OS.

Seven important randomized trials (National Surgical Adjuvant Breast and Bowel Project (NSABP) B-18 (Fisher et al.; Wolmark et al.) [14,15], NSABP B-27 (Bear et al.) [6,10], Mauriac et al. [16], Scholl et al. [17], European Organization for Research and Treatment of Cancer (EORTC) 10902 (van der Hage et al.) [18], Petrov Institute (Semiglazov et al.) [19], and from Royal Marsden (Powles et al.) [20]) have evaluated patients with breast cancer, comparing chemotherapy given either in the preoperative or the postoperative setting. There are difficulties in interpretation because of the variety of different chemotherapy regimens and also wide spectrum of disease stage and trial design. The trials however clearly demonstrate that administration of NACT results in a higher rate of breast conservation when compared to patients receiving chemotherapy in the adjuvant setting. Despite the success of tumor downstaging with NACT, published randomized trials (NSABP B-18 [14,15], NSABP B-27 [6,10], EORTC 10902 (van deer Hage et al.) [18], Petrov Institute (Semiglazov et al.) [19], and from Royal Marsden (Powles et al.) [20]) have so far failed to demonstrate a consistent survival advantage over postoperative chemotherapy.