Research Highlight

Breast conserving therapy

Can Atalay

Department of General Surgery, Ankara Oncology Hospital, Ankara, Turkey

Corresponding to: Can Atalay, MD, PhD. Biskek Cad, Yesiltepe Bloklari, 4. Blok No. 11, Ankara 06510, Turkey. Email: atalay_can@hotmail.com.

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As the awareness of the society on breast cancer and screening for breast cancer increased, more patients with early breast cancer were diagnosed. Attempts to preserve the healthy breast tissue with acceptable oncological and cosmetic outcomes became a challenge for the surgeon. As a result, breast conserving therapy (BCT) has evolved and fundamentally changed the management of early breast cancer. The number of radical surgeries has substantially diminished in the last four decades and a less invasive surgical approach to the breast has replaced mastectomy. Widely acceptance of the concept that breast cancer is a systemic disease at the time of diagnosis played a major role in the evolution of surgical approach to breast cancer. In the beginning, surgeons' approach was more conservative and breast conserving surgery excising larger areas of breast tissue such as quadrantectomy was performed. As the results of related studies were reported, BCT consisting of surgical removal of breast tumor tissue with tumor-free margins and postoperative radiotherapy to the remaining breast tissue became an acceptable therapeutic option. BCT mainly decreased the morbidity resulting from mastectomy such as flap ischemia and necrosis. Thus, adjuvant therapy could be started at an earlier date after surgery.

Long-term results of randomized controlled trials comparing BCT and mastectomy supported the use of limited surgery in early breast cancer (1-10). Milan trial, NSABP B-06 trial, and EORTC 10801 trial are the pioneering trials on the conservative surgical treatment of breast cancer patients. Milan trial included 701 patients with tumors less than 2 cm. Patients were randomized to either radical mastectomy (n=349) or BCT (n=352) (1-3). Quadrantectomy with complete axillary dissection and whole breast radiotherapy with boost dose to the tumor bed were performed in the BCT group. After twenty years of follow-up, local recurrence rate was higher in BCT group compared to radical mastectomy group (8.8% *vs.* 2.3%; P<0.001) (3). On the other hand, overall mortality rate (41.7% *vs.* 41.2%; P=1.0) and breast cancer specific mortality rate (26.1% *vs.* 24.3%; P=0.8) were similar in the two groups (3). In NSABP B-06 trial, more conservative approaches in surgery were evaluated (4-7). Breast conserving surgery was compared to total mastectomy in early breast cancer. In addition, the effect of adjuvant radiotherapy after breast conserving surgery was investigated. A large number of patients (n=1,851) were randomized to total mastectomy (n=589), lumpectomy alone (n=634), and lumpectomy with radiotherapy (n=628) groups. Patients with tumors less than 4 cm were included and lumpectomy was the preferred method of breast conserving surgery. Level I-II axillary dissection was performed in all patients. Whole breast radiation was given as adjuvant therapy in lumpectomy with radiotherapy group; however, boost dose to the tumor bed was omitted. Analysis of patients treated with lumpectomy demonstrated that local recurrence rate is lower when radiotherapy was added after lumpectomy (14.3% *vs.* 39.2%; P<0.001) supporting the concept of BCT. On the other hand, disease-free (P=0.26), distant disease-free (P=0.34), and overall survival (P=0.57) rates were similar between the three groups (7).

In EORTC 10,801 trial, 868 breast cancer patients in stage I/II were randomized to either BCT (n=448) or mastectomy (n=420) (8-10). Patients in this trial had more advanced disease compared to the previous two studies with larger tumors (80%, 2 to 5 cm) and axillary metastases (41%). BCT consisted of lumpectomy, complete axillary dissection, and adjuvant whole breast irradiation with boost dose to the tumor bed. Previous long-term results (median follow-up 13.4 years) demonstrated a higher local recurrence rate in BCT group compared to mastectomy group (11.8% *vs.* 19.7%; HR: 1.64, 95% CI: 1.12-2.38;

P=0.01) (9). Microscopic margin positivity which was detected in 48% of the patients might have a role in higher local recurrence rate after BCT in this trial. Lower local recurrence rate in patients with microscopically tumor-free margins (17.6% *vs.* 26.5%) supports this hypothesis. Positive surgical margins significantly increase the local recurrence rate regardless of postoperative adjuvant treatment. On the other hand, after a median follow-up time of 22.1 years, two groups were comparable in terms of distant metastases (HR: 1.13, 95% CI: 0.92-1.38; P=0.23) and overall survival (HR: 1.11, 95% CI: 0.94-1.33; P=0.23). Twenty-year distant metastases-free survival (46.9% *vs.* 42.6%) and overall survival (39.1% *vs.* 44.5%) rates did not show any significant difference between BCT and mastectomy groups (10).

The long-term results of randomized controlled trials comparing BCT *vs.* mastectomy in patients with early breast cancer have clearly demonstrated that these two treatment modalities are comparable in terms of survival. Although local recurrence rates are higher after BCT, distant disease-free survival and overall survival of the patients treated with either breast conserving surgery or mastectomy are not significantly different. The effect of higher local recurrence rate on systemic disease spread and overall survival is still to be determined. The results of a recent meta-analysis demonstrated that differences in local treatment methods avoid one breast cancer death in 15 years for every four local recurrences avoided in patients with >10% risk of local recurrence (11). Furthermore, loco-regional recurrences showed a negative impact on survival in axillary lymph node positive patients participating in NSABP trials (12). On the contrary, previous analysis of two randomized trials did not report a significant difference in survival between loco-regional recurrences after BCT and mastectomy (13). In addition, with the delivery of better systemic treatments to the patients such as chemotherapy, targeted therapy, and hormonal therapy and with the development of better radiotherapy devices and techniques, the expected rate of loco-regional recurrence decreased from 0.5-1% per year to less than 5% in 10 years. In the future, loco-regional recurrences are expected to decrease further after breast conserving surgery.

As a conclusion, BCT is widely accepted as the gold standard in early breast cancer patients taking into account the patient's choice. There are a number of absolute contraindications to BCT such as inflammatory breast cancer, multicentric disease, pregnancy and previous radiotherapy to the chest wall. Patients with appropriate tumor breast size ratio and without any contraindications can be treated with BCT with acceptable cosmetic results. In addition to preserving breast tissue, less invasive surgical approach to the treatment of axilla is still evolving and will be an important issue in the near future. Eventually, surgery of early breast cancer will be more conservative and less deforming.

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