



After the San Antonio Breast Cancer Symposium 2013

San Antonio Breast Cancer Symposium 2013'ün Ardından

Vahit Özmen

Department of General Surgery, Faculty of Medicine, İstanbul University, İstanbul, Turkey

Dear Colleagues,

The Journal of Breast will be 10 years old in 2014. We have tried to produce an improved, excellent journal with your extraordinary support in this period. I would like to thank all my friends on the editorial board, all reviewers, and our readers and also I would like to wish you all a happy and prosperous New Year.

Dear Readers, I would like to make some comments and explanations regarding the 36th San Antonio Breast Cancer Symposium which was held in San Antonio, Texas in December 10-14, 2013. The symposium continued over 5 days. Tuesday afternoon began with a career development forum for young investigators and educational sessions, together with a variety of presentations on clinical issues. During the subsequent 3 days, there were oral presentations of submitted work in 6 general sessions and 6 poster sessions, as well as selected poster discussions. Interspersed with these were 3 invited plenary talks, several award lectures, 3 mini-symposia, clinical and basic science forums and case discussions. On the 5th day the symposium was brought to a close with a final poster session and the "The Year in Review", which brought together a panel of distinguished speakers whose succinct reports provided a synthesis of major developments in breast cancer during the past year-one of the most popular parts of the program. Some titles of the reports were Screening Mammography, <Local Treatment in Molecular Era, DNA Damage Response as a Target of Therapy, Understanding the Basics of Breast Cancer Diagnosis, Treatment and Clinical Trials Research, HER-2 Translational Research, Global Trends in Breast Cancer Incidence and Mortality, Inflammatory Breast Cancer: Diagnosis, Treatment and Biology, Clinical Science Forum - Management of the Axilla After Neoadjuvant Systemic Therapy, etc (1).

I would like to give you abstracts of two important studies on local treatment and its effects on overall survival in patients with metastatic breast cancer at diagnosis. The first study was presented by Dr. Badwe and the title was "Surgical removal of primary tumor and axillary lymph nodes in women with metastatic breast cancer at first presentation: A randomized controlled trial" (2). The authors studied the effects of surgery in patients with metastatic breast cancer at first presentation in this study.

Background: The role of loco-regional treatment in women with metastatic breast cancer (MBC) at first presentation is debatable. Pre-clinical evidence suggests that such treatment may facilitate growth of metastatic disease. On the other hand, many retrospective analyses in clinical cohorts have suggested a favorable impact of loco-regional treatment in these patients. However, these results are likely to be influenced by selection bias. We conducted a prospective randomized controlled trial to assess the impact of loco-regional treatment on outcome in women with metastatic breast cancer at initial diagnosis. [NCT00193778]

Methods: Women with metastatic breast cancer at initial diagnosis and who were planned to be treated with anthracycline based chemotherapy (CT) were registered for the study. Those who had objective tumor response after 6 cycles of CT were randomized to one of the following arms: loco-regional treatment (LRT) or no loco-regional treatment (No-LRT). Patients were stratified by endocrine receptor (ER) status, site of metastases (visceral Vs bone Vs both) and number of metastatic lesions (<3 vs. >3). Women in the LRT arm received surgery (breast conservation or mastectomy plus axillary lymph node dissection) followed by radiation therapy (RT), as per standard adjuvant guidelines. Women in the No-LRT arm were followed up without surgery and RT. Both groups received standard endocrine therapy after the last cycle of chemotherapy, if indicated. They were regularly followed up with clinical evaluation. Appropriate imaging was performed within 6 months after randomization and thereafter as clinically indicated. The primary endpoint was overall survival (OS).

Address for Correspondence/Yazışma Adresi:

Vahit Özmen, Department of General Surgery, Faculty of Medicine, İstanbul University, İstanbul, Turkey
Phone / Tel.: +90 532 215 07 77 e-mail / e-posta: vozmen@istanbul.edu.tr

Results: Between Feb 2005 and Jan 2013, 350 women were randomized, 173 in the LRT and 177 in the No-LRT arms. The data cutoff was in May 2013. The two arms were balanced with respect to age, clinical tumor size, HER2 receptor status and stratification factors. Eight (5.8%) patients in the LRT arm did not undergo loco-regional therapy while 19 (10.7%) patients in the No-LRT arm underwent surgical removal of the primary tumor due to palliative reasons. The median follow-up was 17 months and 218 deaths (LRT=111/173, No-LRT=107/177) had been recorded at data cutoff. The median OS in the LRT and No-LRT arms were 18.8 and 20.5 months (HR=1.07, 95% CI=0.82-1.40, p=0.60) and the corresponding 2-year OS were 40.8% and 43.3%, respectively. After adjusting for age, ER status, HER2 receptor status, site of metastases and number of metastatic lesions in a Cox regression model, there was no significant difference in OS between the LRT and No-LRT arms (HR=1.00, 95%CI=0.76-1.33, p=0.98). There was no interaction between the effect of LRT and covariates in the model.

Conclusions: Loco-regional treatment of the primary tumor and axillary nodes has no impact on OS in patients diagnosed with MBC at initial presentation, who have responded to frontline chemotherapy. We were unable to identify any subgroups that are likely to benefit from LRT. Such treatment should be reserved for women who need it for palliative reasons. Detailed analysis will be presented at the Symposium.

The authors tried to explain these negative results with Fisher's animal study in mice (3). In his study, tumor growth factor was found responsible for metastatic tumor progression in mice after excision of the primary tumor. The advanced level of metastatic breast cancer at presentation, lack of modern systemic treatment in most patients, and insufficient follow-up time were weaknesses of the study.

The second important prospective randomized study presented in SABCS was performed by the Turkish Federation of Breast Disease Societies with a title of "Early follow up of a randomized trial evaluating resection of the primary breast tumor in women presenting with de novo stage IV breast cancer; Turkish study (protocol MF07-01)" (4). This is the first time a study performed in Turkey has been orally presented in SABCS. The abstract of the study presented by Dr Soran was Introduction: Previous reports of carefully selected patients presenting with stage IV breast cancer (BC) suggest that surgery on the primary tumor may result in improved survival, but this remains unproven. The MF07-01 trial is a phase III randomized controlled trial of BC women with distant metastases at presentation who receive loco-regional (LR) treatment for intact primary tumor compared with those who do not receive such treatment.

Aim: The primary objective of the trial is to compare overall survival (OS) in women treated with or without initial LR resection prior to systemic therapy for de novo stage IV BC.

Materials and Methods: At the discretion of the surgeon, LR treatments consisted of either mastectomy or breast conserving surgery with level I-II axillary clearance in clinically or sentinel lymph node positive patients. Radiation therapy to the whole breast was required following breast conserving surgery. At the discretion of the medical oncologist, standard systemic therapy of either endocrine treatment or chemotherapy (plus trastuzumab for HER2 +) was given to all patients either immediately after randomization (no surgery group) or after surgical resection of the intact primary tumor (surgery group).

After consideration of previous retrospective studies, the assumed OS difference between the two groups was determined to be 18% (35% in LR treatment group versus 17% in no-LR treatment group). A 10% drop out rate including 'lost to follow up' was assumed. By using a one sided log-rank test with a 95% confidence ($\alpha=0.05$) and a 90% power ($\beta=0.9$), sample size calculation revealed that 271 patients were needed to be randomized.

Results: There were 140 women in the surgery group and 138 in the no-surgery group. The mean follow up time was 21.1+14.5 months. The mean age was 51.6+13.2 years and the groups were comparable regarding age, BMI, ER/PR, Her 2, Triple negative, tumor type and size (all p>0.05). Metastatic patterns included bone only in 45.7%, organ except bone in 28.8%, and bone plus organ in 25.5%. There were a total of 86 (31%) deaths. At 54 months the survival rate was 35% in the surgery group and 31% in the no surgery group (p=0.24). However, OS was statistically higher in bone only, ER/PR positive and patients younger than 50 years but was lower in the triple negative patients (p<0.05). The mean survival was 7.1 months higher in the surgery group compared with the no surgery group in bone only metastasis (39.1+1.8 vs 32.0+2.2; p=0.13). Surgery in the group of patients who had solitary bone only metastasis had statistically significant survival benefit compared with no surgery and with patients who had multiple bone metastasis either with or without surgery (p=0.03).

Conclusion: In the early follow-up of this trial comparing surgery of the primary tumor with no surgery in stage IV BC at presentation, OS was similar but there were important subgroup differences; in particular those with solitary bone metastasis have a significant survival benefit and patients with bone metastasis only have a trend toward improved survival with initial surgery. Further follow-up will expand on these important findings. The weak side of the study was lack of biopsy in patients with solitary bone metastasis, and short median follow-up time.

Two studies from Bahcesehir Breast Cancer Screening Study were also presented in this symposium, and I would like to present their abstracts to inform you of this important prospective study. The first poster was presented by Dr. Ozmen and Dr. Ozcinar with a title of Successful results of a population-based organized mammography screening program in a developing country: The Turkish experience (5).

Objective: This study aims to determine the feasibility of a population-based organized mammography screening in a developing country (Bahcesehir, Istanbul, Turkey) and to determine the starting age for screening.

Materials and Methods: Women aged 40-69 were invited for screening at 2-year intervals starting in January 2009. Digital 2-view mammograms were obtained, and mammograms were double read by two independent radiologists who were experienced in breast imaging. The women were recalled in consensus for additional work-up, including spot compression/magnification mammograms or breast ultrasound. Outcomes were measured from final assessment or histopathologic confirmation. The participation rate for second round, recall rate, number of biopsies, the women diagnosed with cancer and patient and tumor characteristics were evaluated.

Results: Between January 2009 and January 2013, 5938 (89.4%) of 6640 women aged between 40-69 years old accepted the mammographic invitation. Most of them (58%) were in the 40-49 age group, and the average 2-year attendance for second rounds were 82.6% and

81.2%, respectively. Spot recall rates were 16.8% and 25.6% for the first and second rounds, respectively. Core biopsy was required in 108 patients (1.8%), whereas BC was diagnosed in 50 patients (0.84%). Twenty-four patients (48%) detected with BC were in the 40-49 age group. There were 39 patients (78%) with invasive BC and 11 patients (22%) with ductal carcinoma in situ (DCIS). Stages of 39 patients with invasive BC were Stage I (n=26; 52%), II (n=10; 20%) and III (n=3; 6%), respectively. The majority of patients (88%) had breast conserving surgery, and sentinel lymph node biopsy only (72%) as the axillary procedure. Of invasive cancers, 92% were found to be hormone receptor positive, and 59% had low Ki67 levels (≤ 15). However, HER2-neu positivity (8%) along with triple negative cancers (3%) were less frequently detected.

Conclusion: These findings supports the prevailing view that mammographic screening increases early breast cancer detection rate, which has a less aggressive biology. Screening mammography program can be successfully implemented in a developing country, e.g Turkey. However, more experienced dedicated breast cancer screening teams and continuous, increasing efforts are required to decrease our relatively high recall rates. These results showed the organized mammographic screening in Turkey as a developing country. However, recall rates were high, and should be decreased.

The second poster presentation from Bahcesehir Screening Project was presented by Dr. Cabioglu (6). The abstract was:

Objectives: Turkish Bahcesehir Breast Cancer Screening Project is a 10-year organized population based screening program carried out in one of the largest counties of Istanbul, Turkey. The aim of our study is to examine the biological features of screen detected breast cancers detected during the initial 4-year study period as an interim analysis.

Study Design and Methods: Between January 2009 and May 2013, a total of 6298 women aged between 40-69 years were recruited in this prospective study. Two-view mammographies were obtained at 2-year intervals, and classified according to Breast Imaging Reporting and Data System of the American College of Radiology (ACR). Clinicopathological and biological tumor characteristics were analysed for those diagnosed with breast cancer. Tumors were stained for estrogen (ER) and progesterone receptors (PR), HER2-neu and Ki-67 by immunohistochemistry.

Results: A total of 57 breast cancers (0.9%) were detected during the study period. The median age was 50 (40-70). The majority of patients (72%) were stage 0 or 1, whereas 28 patients (49%) were < 50 age. Of 57 tumors, 45 (79%) were invasive cancers and 12 (21%) were ductal carcinoma in situ. Forty-eight patients (86%) underwent breast con-

servation, whereas 37 patients (65%) had sentinel lymph node biopsy only as the axillary procedure. Of the 45 invasive cancers, 31 (69%) were ductal carcinoma and 8 (18%) were pure lobular carcinoma. Among 45 invasive cancers stained for ER, PR, HER2-neu and Ki67, the majority (91%) were ER or PR receptor positive, whereas 11% were HER2-neu positive and 58% had low Ki67 levels (< 15). As molecular subtypes, the majority of them were found to be either luminal A (57%) or luminal B type (34%), whereas other nonluminal HER2 (4%) and triple negative cancers (5%) were less frequently detected.

Conclusions: Our findings suggest that the majority of screen-detected breast cancers exhibit either luminal A or B subtype. However, more aggressive subtypes, such as nonluminal HER2-neu or triple negative cancer, are less likely to be detected by mammographic screening programs, requiring other preventive strategies. According to the results, breast cancers detected during screening mammography have excellent prognostic factors and better luminal subtypes.

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