

EVALUATION AFTER 13TH ST. GALLEN BREAST CANCER CONFERENCE “ADVANCES IN EARLY BREAST CANCER SURGERY: BREAST CONSERVING SURGERY (BCS) AND SENTINEL LYMPH NODE BIOPSY (SLNB)”

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In this issue, I would like to give you some short information about 13th St. Gallen Breast Cancer Conference and Surgical Panel in which I attended.

The conference was held on March 13-16, 2013 in St. Gallen, Switzerland and consisted of 10 panels and 5 satellite symposiums and a consensus panel which was lasting for 4 hours in the last day of the conference. The conferences were planned to be held out of St. Gallen henceforth, and will be held at Vienna in 2015.

Similar to the St Antonio Breast Cancer Symposium, in this meeting in addition to molecular biology in breast cancer, targeted therapies, molecular subtypes, and triple negative breast cancer, personalization of physical activities and nutrition, obesity, endocrine treatment, high risk groups, screening, diagnosis, pathological examination, and adjuvant systemic treatments were discussed in this conference. There were two separate panels on surgical treatment and radiotherapy which are local treatments of breast cancer.

The only panel on surgery in breast cancer entitled “Advances in surgical management of early breast cancer” was performed under the chairmanships of Dr. John Forbes from Australia and Dr. Michael Gnant from Austria. The speakers and their subject headings are listed below:

- How to handle positive sentinel nodes? (Viviana Galimberti, Italy)
- Oncoplastic and reconstructive surgery of the breast (Moustapha Hamdi, Belgium)
- Personalizing extent of breast cancer surgery according to molecular subtypes (Monica Morrow, USA)
- Who should not undergo breast conservation? (Emiel J T Rutgers, Netherlands)
- Close/positive margins after breast-conserving therapy: Additional resection or no resection? (William Wood/USA)

As a first speaker, Dr. Galimberti explained the study, which was published in Lancet Oncology last month, entitled “Axillary dissection versus no axillary dissection in patients with sentinel-node micrometastases (IBCSG 23-01): a phase 3 randomized controlled trial” (1). In that study, patients who were diagnosed with cT1,2N0

breast cancer and had micrometastases detected by SLNB were randomly assigned into two groups as the group undergoing axillary dissection (AD) (n=465) and other group as not undergoing AD (n=469). There were no significant differences between two groups regarding 5-year disease-free survival (DFS) and overall survival (OS). Consequently, AD should be avoided in patients who underwent BCS and had micrometastases after SLNB. Moreover, the rate of patients who underwent mastectomy was low (9%) and no results were obtained whether they underwent AD after micrometastases or not. However, Dr. Galimberti, referred to another study by Sarah et al. published in the last year in the Annals of Surgical Oncology (2). In that study, the patients with positive sentinel lymph node (SLN) who did not undergo AD and the patients who underwent total mastectomy and BCS were randomized. After 57.8 months median follow-up, the rates of 4-year local, regional, and distant organ metastases were found to be similar and it was reported that in patients with minimal SLN involvement and who did not undergo AD, mastectomy or BCS did not affect prognosis.

Dr. Galimberti stated that the results of the ACOSOG Z0011 study which recommended to avoid AD in 1-2 SLN positive patients and criticized that particular study as only reaching the half of the targeted number of patients, being difficult to assess the little difference among groups, reporting two times more common axillary recurrence in the no-AD group, and lack of identifying the number of the remaining involved lymph nodes due to not performing AD (3). Despite these weaknesses, similar OS and DFS between the groups, higher local recurrence in the no-AD group than the AD group, and adjuvant systemic treatment of axillary involvement were the strengths of the study. Dr. Galimberti gave two important messages: 1- A positive SLN does not require further treatment in early stage breast cancer with clinically negative axilla, 2- The decision should consider patient’s age and preference, and other concomitant conditions.

Dr. Moustapha Hamdi (plastic surgeon) gave a speech on the topic entitled “Oncoplastic and reconstructive surgery of the breast” and gave information about techniques and practices of “oncoplastic surgery (OPS)” which has an important role in breast cancer surgery, especially in the last decade (4). Partial breast reconstruction that is performed immediately after large tumor excision has been

defined as OPS. In these patients before OPS, mastectomy was performed or cosmetic appearance was bad in performed BCSs. Performing different techniques according to sizes of breast and tumor, good cosmetic outcome can be obtained and local recurrence can be decreased by supplying wider surgical margin. Most frequently used flaps indicated by Dr. Hamdi were mini or large latissimus dorsi flaps, and perforator flaps (thoracodorsal perforator flap [77%], lateral intercostal artery perforator flap, and serratus anterior artery perforator flap).

Dr. Monica Morrow gave a speech entitled "Personalizing extent of breast cancer surgery according to molecular subtypes" and stated that biological factors [histology, grade, nodal status, estrogen receptor (ER), human epidermal growth factor receptor-2 (HER-2)] and mechanical factors [extent of disease in breast, negative margins, diffuse microcalcifications, multicentricity, and inability to take radiotherapy (RT) (prior RT, systemic lupus, scleroderma)] play roles in BCS selection. When OS and DFS were observed according to molecular subtypes, the luminal A group had the best results, followed by luminal B, normal like, basal like, and HER-2 positive groups (5, 6). The rates of multifocal/multicentric cancer and extensive intraductal component (EIC) were higher in the HER-2 positive group. When local recurrence was observed according to molecular subtypes after BCS and mastectomy, maximum local recurrence was obtained in the triple negative and HER-2 positive groups. Treatment with trastuzumab decreased local recurrence rate (LRR) from 7% to 1% in HER-2 positive patients (7). In triple negative patients, performing mastectomy instead of BCS does not decrease local recurrence. Consequently, Dr. Morrow emphasized that local-regional recurrence changed with molecular subtypes, that greater surgery could not overcome unfavorable biology, and that increasing activity of multimodal treatment options and especially systemic therapy decreased local recurrence and surgical morbidity.

Dr. Monica Morrow pointed out two studies which investigated factors affecting axillary local recurrence and mentioned that diameter of axillary metastatic lymph node, histologic grade, number of involved lymph node, and adjuvant treatment were important prognostic factors (8, 9). She indicated that, in the ACOSOG Z0011 study, patients with cT1-2, N0 who underwent BCS and had a positive SLNB were randomly assigned to AD and no-AD groups and were administered systemic therapy and RT and that the outcomes after median 6.3 years follow-up revealed no difference between the AD and SLNB groups in terms of local recurrence, OS, and DFS (3). It was critically emphasized that patients included in that study had good prognosis and were well selected and that the results were not valid for all patients who underwent BCS. Consequently, it was summarized that age, ER, and positive HER-2 could not be predictive factors for AD need and that longer follow-up was needed to determine the frequency of axillary recurrence.

In the speech of Dr. Emiel J. T. Rutgers entitled "Who should not undergo breast conservation?", he re-discussed indications of BCS. He listed the proven risk factors for local recurrence in breast cancer as inadequate excision (invasive or ductal carcinoma in situ), not receiving RT, young age (<35), and tumor biology (BRCA1/2 positiv-

ity) and emphasized that 25% of women preferred mastectomy in different studies (10). The factors that determine local recurrence were tumor biology, imaging methods, surgery, pathology, radiotherapy, and systemic therapy. Currently, it is known that LRR for a successful BCS should be <1% per year. For local recurrence, surgical margin being close (no ink on tumor) or negative is not important; however the surgical margin should not be positive. Finally, it is stated that young age (<35), diffuse microcalcifications (if not its positivity was proven pathologically), multifocality, multicentricity in some cases, cancer close to nipple, diffuse lymphovascular invasion and intraductal component, lobular pathology, and positive family anamnesis are not contraindicated with BCS. However, positivity in surgical margins, not receiving RT, and patient's preference for mastectomy are contraindicated with BCS.

The last speaker was Dr. William Wood and in his speech entitled "Close/positive margins after breast-conserving therapy: Additional resection or no resection?", he discussed "how distant should the margin of BCS be?". Dr. Wood presented studies in which no differences were obtained between negative margin (> 1 mm) and close margin (\leq 1 mm, no ink on tumor) in terms of local recurrence and he emphasized that 4 mm margin decreased to 1 mm when the specimen was examined pathologically (11, 12). He referred to a study conducted in Netherlands which indicated the determination of the surgical margins by intra-operative ultrasonography decreased the re-excision rate 5 times and he mentioned a device which detected surgical margin electromagnetically and was on testing stage (13). He pointed out that diagnosis should be performed with pre-operative tru-cut biopsy, that factors such as tumor size and biology, age, multifocality, breast volume, and localization of tumor in the breast should be considered together, that positive surgical margin should be re-excised, and that re-excision was not required in close surgical margin.

When we evaluate speeches on the indications of BCS, we realize that indications of BCS have been expanded and multicentric cancer, young age, lobular histology, tumor/breast ratio, and tumor biology are not contraindications for BCS from now. Additionally, >2 mm clear margin recommended insistently for BCS before was also decreased to >1mm or close margin. Herein, the important issue is the absence of tumor cell at surgical margin and absence of ink on tumor after dying excised specimen. This result can be reached with above-mentioned clinical studies and meta-analyses and it is concluded that close or distant surgical margin do not indicate significant differences in local recurrence in long-term follow-ups. The most important reasons of increase in the indications of BCS and decrease in LRR (<1% per year) can be explained by the decrease in tumor diameter, better tumor biology, and efficacies of RT (+boost) and systemic therapy. The evaluation of axilla and determination of axillary involvement, which are the most important prognostic factors of breast cancer, have been losing their importance. While, the ACOSOG Z011 study recommended not to perform AD in patients who underwent BCS and had 1-2 SLN positive, the IBCSG 23-01 study recommended not to perform AD in patients who were detected with micrometastasis and had SLN. However, larger randomized clinical studies are needed in order not to use SLNB and AD.

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