



SPECIAL ARTICLE

Meeting Highlights: The Second Consensus Conference for Breast Cancer Treatment in Korea

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The Korean clinical practice guideline recently developed by the Korean Breast Cancer Society to address the national clinical situation is currently under revision ahead of a seventh recommendation. A second consensus conference was held to further develop this guideline by soliciting opinions regarding important issues related to surgery, radiotherapy, and medical oncology. Several issues were discussed, and the discussion progressed to pros and cons in the context of cases in various clinical situations. The panels discussed and voted on issues regarding surgical treatment for non-axillary regional lymph nodes, regional nodal irradiation of pN1 disease, and ovarian functional suppression (OFS) as an adjuvant treatment in premenopausal patients with hormone receptor-positive breast cancer. Regarding the surgical treatment of non-axillary regional lymph node, most panelists agreed with the recommendation of preoperative che-

motherapy and postoperative radiotherapy for patients with biopsy-diagnosed metastases, whereas surgery or radiotherapy of non-axillary regional lymph nodes was suggested for clinical partial responders. Discussions on radiotherapy addressed the need for adjuvant radiotherapy and radiation field of regional lymph node in the context of various N1 breast cancer cases. The participants reached a consensus to recommend that N1 patients should receive regional nodal irradiation for a large tumor burden (e.g., three positive nodes, perinodal extension, or large primary tumor). Finally, the panels favored OFS in addition to endocrine therapy for premenopausal women with high risk factors such as a large tumor size, involvement of more than three nodes, and a high histologic grade.

Key Words: Breast neoplasms, Consensus, Interdisciplinary communication

INTRODUCTION

According to the national cancer statistics from 2013, breast cancer is the second most common cancer affecting women in Korea. Encouragingly, the 5-year breast cancer survival rate increased by 13.6% from 77.9% during 1993–1995 to 91.5% in 2013 due to early diagnosis and updated treatment. This survival rate seems almost second-to-none among developed

countries worldwide [1]. Furthermore, the nationwide survey and breast cancer registry database of the Korean Breast Cancer Society indicated a rapid increase in breast cancer incidence until 2010, followed by a gradual stabilization [2].

The Korean Breast Cancer Society has recently developed a Korean clinical practice guideline in response to the need for a more standardized and updated guideline based on the principle of a multidisciplinary approach to breast cancer treatment within the current Korean clinical situation. This guideline is currently under revision, leading to the seventh recommendation. A second consensus conference was subsequently held to further develop this guideline and progressed to pros and cons. The conference panel involved 43 experts, including 16 medical oncologists, 16 surgeons, two pathologists, two radiologists, and seven radiation oncologists from whom opinions were solicited regarding important issues re-

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lated to surgery, radiotherapy, and systemic treatment/medical oncology. The panel covered three areas, namely, surgery, radiotherapy, and systemic treatment. First, surgical treatment for non-axillary regional lymph nodes was discussed, followed by a panel discussion on regional nodal irradiation in patients with pN1 disease. Regarding systemic treatment, the panel members discussed whether to recommend ovarian functional suppression (OFS) as an adjuvant treatment in premenopausal patients with hormone receptor-positive breast cancer. The details of the recommendations regarding treatment decisions related to these issues are provided in Supplementary Table 1 (available online).

CONFERENCE HIGHLIGHTS: PANEL DELIBERATION

Surgical treatment issues: is surgery recommended for non-axillary regional lymph node?

In this conference, we discussed the surgical management of non-axillary regional lymph nodes, which we defined as the internal mammary and supraclavicular lymph nodes. We discussed the case with no distant metastasis. For cases involving suspicious non-axillary regional lymph nodes, approximately 42% of the panelists answered that they would perform fine-needle aspiration or gun biopsy to confirm an internal mammary node metastasis (Q1-1), whereas more panelists agreed with biopsy of a suspicious supraclavicular lymph node during the staging evaluation (Q1-2). For patients with suspicious non-axillary regional lymph nodes, most panelists agreed with the recommendation of preoperative chemotherapy (65.9% for the internal mammary lymph node and 78% for the supraclavicular lymph node) (Q1-3, Q1-4). Furthermore, more panelists agreed with preoperative chemotherapy if the lymph node metastasis had been confirmed via biopsy (fine-needle aspiration or gun biopsy) (Q1-5, Q1-6).

Most panelists did not include the non-axillary regional lymph node during surgery if a clinically complete response had been achieved in this node after preoperative chemotherapy for a biopsy-confirmed metastasis (Q1-7, Q1-8). For cases involving a clinical partial response in a biopsy-confirmed metastasis to the internal mammary lymph node, approximately half of the panel surgeons stated that they would include those nodes during mastectomy surgery (Q1-9-2), whereas a large proportion of surgeons would include supraclavicular lymph nodes with biopsy-confirmed metastasis during surgery (Q1-10-1, Q1-10-2). Finally, most panelists agreed with postoperative radiotherapy for patients with biopsy-confirmed non-axillary regional lymph node metastasis, regardless of extent of the response to neoadjuvant chemo-

therapy (Q1-13, Q1-14, Q1-15).

Radiation treatment issues: who could benefit from irradiation of N1 breast cancer?

Regarding breast cancer patients with pN1 disease who underwent breast-conserving surgery, 71.8% of the panelists answered that regional nodal irradiation would be unnecessary. However, most (97.4%) still believed that irradiation should be performed for young patients and patients with high-grade disease, lympho-vascular invasion (LVI), a high positive lymph node ratio, positive lymph node number, extracapsular extension, and/or a triple-negative breast cancer status.

Most panelists (85.2%) considered the tangential field to be sufficient for low-risk patients undergoing radiotherapy for one positive node. However, 53.2% to 56.7% favored the inclusion of a regional lymph node along with the tangential field if the risk of regional recurrence had increased because of three-node or hormone receptor-negative disease with node positivity. The range of regional nodal irradiation was classified as including the supraclavicular lymph node only or including both the supraclavicular and internal mammary lymph nodes.

For cases with a positive sentinel lymph node that had not undergone axillary lymph node dissection, the majority (63.3%) of participants voted that radiotherapy including the regional lymph node should be considered without additional surgery, whereas 26.7% considered axillary lymph node dissection followed by tangential irradiation to be superior.

Regarding pT3N1 cases treated with mastectomy, 81.1% agreed that all patients should undergo radiotherapy for the regional node. However, most panelists also agreed that additional radiotherapy may not be necessary for pT2N1 cases, although 42.5% stated that adjuvant radiotherapy should be performed for high-risk patients in this group (e.g., three positive nodes).

For mastectomy cases with positive sentinel lymph node biopsies, 43.7% of the panelists reported that postoperative axillary radiotherapy would be sufficient without axillary lymph node dissection, whereas (56.3%) voted that axillary lymph node dissection should be performed with mastectomy.

Systemic treatment issue: is ovarian function suppression recommended for premenopausal patients with hormone receptor-positive breast cancer in an adjuvant setting?

Before the panel discussion, two speakers reviewed the background knowledge regarding OFS use in hormone receptor-positive premenopausal women in terms of the pros and cons considering the results of two large randomized phase III trials, namely, the Suppression of Ovarian Function Trial

(SOFT) [3] and the Tamoxifen and Exemestane Trial (TEXT) [4]. The panel considered treatment recommendations for eight clinical scenarios involving cases of hormone receptor-positive and human epidermal growth factor receptor 2 (HER2)-negative disease at diagnosis. The first case (Q3-1) involved a 40-year-old woman with a grade 3, T1, node-positive tumor who developed intermittent menses after adjuvant chemotherapy. Approximately half of the panel (48.4%) agreed that this patient should receive tamoxifen with OFS. The next case (Q3-2) had the same biologic characteristics but node-negative disease and remained in premenopausal status after adjuvant chemotherapy. In this case, an overwhelming majority of the participants (87.1%) would not advise OFS for this patient. The third case involved a premenopausal woman with node-negative disease and a low-grade tumor who had not received adjuvant chemotherapy (Q3-3). Again, the majority of participants (71.9%) would not advise the combined use of OFS with tamoxifen for this patient. The fourth case (Q3-4) involved a 40-year-old patient with T2N1M0, grade 3 disease, who did not have regular menses after adjuvant chemotherapy and presented with a serum estradiol level of 10 pg/mL and follicle-stimulating hormone level of 18 mIU/mL. More than half (58.6%) of the panel recommended tamoxifen monotherapy for this patient.

For the fifth case (Q3-5), we used the situation from the fourth case but assumed that menstruation resumed during tamoxifen treatment to determine the impact of regular menses on decisions regarding OFS use. Again, a little more than half of the panel (53.3%) advised against adding OFS to tamoxifen. The next two scenarios (Q3-6, Q3-7) involved a 35-year-old woman with T2N2M0, grade 3 disease who received adjuvant chemotherapy followed by tamoxifen and OFS. The current Korean National Insurance Service guideline allows OFS treatment for up to 2 years in an adjuvant setting and does not coverage combination therapies comprising an aromatase inhibitor plus OFS for premenopausal patients. When asked not to consider the Korean National Insurance Service guideline, a majority of participants (73.3%) agreed that they would continue the regimen of OFS and tamoxifen after 2 years (Q3-6). However, when the guideline was considered (Q3-7), few participants (55.2%) preferred to continue OFS and tamoxifen combination therapy for this patient, and less than 10% of the panel recommended the use of aromatase inhibitor (AI) with OFS. The last case (Q3-8) involved a 35-year-old woman with clinically T3N2M0, grade 3 disease. Although her tumor shrank to ypT1N1M0 after neoadjuvant chemotherapy, the pathology changed to estrogen receptor negative. Still, a majority (64.3%) of participants reported that they would select OFS with tamoxifen as an adjuvant endo-

crine therapy for this case.

In summary, the panels favored OFS in addition to endocrine therapy for premenopausal women with high risk factors, such as a large tumor size, involvement of more than three nodes, and a high histologic grade. Despite the superior results of AI plus OFS in this high-risk group, the panel preferred tamoxifen, rather than AI, in combination with OFS. Furthermore, the majority of participants agreed to maintain OFS treatment for up to 5 years for high-risk patients. However, the extended use of OFS (more than 5 years) was not addressed at this conference.

DISCUSSION

Surgical treatment issues

Although debates regarding the surgical treatment of non-axillary regional lymph nodes continue, most of the panelists at this conference agreed with the use of preoperative chemotherapy and postoperative radiotherapy for patients with biopsy-confirmed metastases. Furthermore, many participating surgeons would consider surgical treatment for lymph nodes in cases involving clinical partial responses. Here, more surgeons selected additional surgery for proven non-axillary node metastases for cases involving the supraclavicular nodes, rather than the internal mammary nodes, those involving partial rather than complete responses to neoadjuvant chemotherapy, and those involving mastectomy rather than breast conservation surgery after preoperative systemic therapy. However, some surgeons also discussed the benefits of radiotherapy for patients who achieved a partial response. These responses suggest that treatment decisions for such patients should be discussed in a multidisciplinary team setting.

Radiotherapy issues

For breast cancer cases involving one to three positive pathologic lymph nodes, the primary issues involve the selection and the range of radiotherapy and radiation treatment. According to recently published results from the National Cancer Institute of Canada Clinical Trials Group MA.20 and EORTC 22922 trials, regional nodal irradiation significantly increased disease-free survival (DFS) among patients with breast cancer who underwent breast-conserving surgery [5,6]. Studies of regional nodal irradiation can be classified according to whether patients underwent breast-conserving surgery or mastectomy. For the former, the whole breast is subjected to regional nodal irradiation, whereas with the latter, the chest wall is irradiated [7]. Regional nodal irradiation usually extends to the axillary apex and supraclavicular fossa, although the involvement of the internal mammary lymph node re-

mains controversial [8].

In previous Danish and British Columbian trials, postmastectomy radiotherapy (PMRT) significantly reduced the locoregional recurrence rate and increased survival among patients with one to three positive nodes [9,10]. In 2014, the Early Breast Cancer Trialists' Collaborative Group performed a meta-analysis of 8,135 patients in 22 randomized trials. Among the 1,314 patients with one to three positive nodes, the addition of PMRT resulted in a decrease of the 10-year locoregional recurrence rate from 20.3% to 3.8% ($p < 0.00001$) [11]. The 10-year recurrence rate also decreased from 45.7% to 34.2% ($p = 0.00006$), although the 20-year breast cancer mortality rate increased from 42.3% to 50.2% ($p < 0.001$).

However, the benefits of PMRT for pN1 patients remain controversial, as these patients have a relatively low risk of locoregional recurrence. Furthermore, recent therapeutic advances and increased biologic knowledge have reduced the benefits of PMRT for pN1 patients [12,13]. Chang et al. [14] found that PMRT significantly increased the DFS in a cohort of recently treated pN1 patients (2004–2011). Their findings suggest that the potential benefits of PMRT should still be considered, despite advances in surgical and systemic treatments. However, our investigation found that only 11.9% of Korean women with T1–2N1 breast cancer actually received PMRT [15]. In this consensus conference, 80% of the panelists answered that they would not advise additional radiotherapy, similar to the current clinical practice situation. The panelists also stated that N1 patients should undergo regional nodal irradiation for a large tumor burden (e.g., three positive nodes), perinodal extension, or a large primary tumor ($\geq T3$).

Although several studies found that risk factors such as high-grade tumors, estrogen receptor negativity, young age, high positive nodal ratio, medical location, close margins, and LVI could reduce survival [13], the definitions of these factors are heterogeneous. Therefore, whether the outcomes of regional node radiotherapy are affected by risk factors remains unclear. The multicenter KROG 14-23 study investigated risk factors for recurrence in patients with N1 disease after recent systemic therapy without PMRT [16]. In this study, patients were grouped according to the number of risk factors with the aim of defining a subgroup that might benefit from PMRT. The results of the SUPREMO trial, a large randomized trial on the benefit of PMRT, might better stratify patients and identify those who should undergo PMRT [17].

The panelists further addressed the issue of subsequent treatment for patients who underwent mastectomy and had a positive sentinel lymph node biopsy. Here, 43.7% of the panelists considered axillary radiotherapy without axillary lymph node dissection to be sufficient. By contrast, 57.6% of the pan-

elists from the first Korean Breast Cancer Treatment Consensus conference answered that radiotherapy could replace additional axillary lymph node dissection [18]. This discrepancy is attributed to differences in wording, as the relevant question at the first conference concerned patients who had undergone breast conserving surgery or mastectomy. Therefore, additional time may be needed before clinicians accept the use of radiotherapy without additional axillary lymph node dissection, despite studies such as ACOSOG Z0011 and the AMARO trial [19,20].

Systemic treatment issues

For systemic treatment issues regarding OFS as an adjuvant treatment in patients with hormone receptor-positive premenopausal breast cancer, speakers mainly discussed and progressed to pros and cons regarding the results of two large randomized phase III trials, namely, the SOFT [3] and TEXT [4]. The TEXT was designed to compare 5 years of tamoxifen therapy plus OFS versus exemestane plus OFS, whereas the SOFT was a three-arm trial in which 5 years of tamoxifen monotherapy was compared with tamoxifen plus OFS and exemestane plus OFS. A pooled analysis of the TEXT and SOFT results showed that the combined administration of an aromatase inhibitor with OFS significantly improved the 5-year DFS when compared with tamoxifen plus OFS (hazard ratio [HR], 0.72; 95% confidence interval [CI], 0.60–0.85; $p < 0.001$). In the SOFT trial, the addition of OFS to tamoxifen did not improve DFS when compared with tamoxifen monotherapy. However, this combined regimen provided a significant benefit relative to tamoxifen alone for women with risk factors for recurrence, such as lymph node metastasis and an age younger than 35 years (HR, 0.78; 95% CI, 0.62–0.98).

Until recently, tamoxifen was considered the standard chemotherapeutic for premenopausal women with early hormone receptor-positive breast cancer. However, the results from the TEXT and SOFT have led clinicians to more frequently consider the addition of OFS to adjuvant tamoxifen or AI treatment in this population. The ECOG trial 3193 [3], a randomized phase III trial of tamoxifen monotherapy versus tamoxifen plus OFS in patients with hormone receptor-positive, node-negative disease and tumor sizes ≤ 3 cm, failed to demonstrate the clinical benefit of OFS, and the lack of a significant benefit of OFS was repeatedly confirmed in low-risk cohorts. By contrast, the SOFT demonstrated a substantial benefit of OFS, that is, a reduced risk of recurrence, in a high-risk cohort of breast cancer patients. The present conference panelists acknowledged that OFS could aggravate symptoms, such as hot flashes and sexual dysfunction, and may reduce the quality of life. Accordingly, they expressed great concern

regarding the toxicities associated with AI plus OFS regimens in young patients. Therefore, the panel recommended that the pros and cons of OFS be communicated to patients during the decision-making process.

CONCLUSION

Although an evidence-based recommendation was made, the panel had different opinions in various contexts. Discussions regarding the surgical treatment of non-axillary regional lymph node included issues related to surgery or radiotherapy. Radiotherapy issues were further discussed with respect to the need for additional radiotherapy and the radiation field used to target regional lymph nodes in patients with N1 breast cancer. Furthermore, the panelists favored the administration of OFS in addition to endocrine therapy for premenopausal women with high risk factors, such as a large tumor size, involvement of more than three nodes, and a high histologic grade.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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REFERENCES

1. Oh CM, Won YJ, Jung KW, Kong HJ, Cho H, Lee JK, et al. Cancer statistics in Korea: incidence, mortality, survival, and prevalence in 2013. *Cancer Res Treat* 2016;48:436-50.
2. Min SY, Kim Z, Hur MH, Yoon CS, Park EH, Jung KW, et al. The basic facts of Korean breast cancer in 2013: results of a nationwide survey and breast cancer registry database. *J Breast Cancer* 2016;19:1-7.
3. Francis PA, Regan MM, Fleming GF, Láng I, Ciruelos E, Bellet M, et al. Adjuvant ovarian suppression in premenopausal breast cancer. *N Engl J Med* 2015;372:436-46.
4. Paganì O, Regan MM, Walley BA, Fleming GF, Colleoni M, Láng I, et al. Adjuvant exemestane with ovarian suppression in premenopausal breast cancer. *N Engl J Med* 2014;371:107-18.
5. Whelan TJ, Olivetto IA, Parulekar WR, Ackerman I, Chua BH, Nabid A, et al. Regional nodal irradiation in early-stage breast cancer. *N Engl J Med* 2015;373:307-16.
6. Poortmans PM, Collette S, Kirkove C, Van Limbergen E, Budach V, Struikmans H, et al. Internal mammary and medial supraclavicular irradiation in breast cancer. *N Engl J Med* 2015;373:317-27.
7. Park SH, Kim JC, Lee JE, Park IK. Virtual lymph node analysis to evaluate axillary lymph node coverage provided by tangential breast irradiation. *Radiat Oncol J* 2015;33:50-6.
8. Hennequin C, Bossard N, Servagi-Vernat S, Maingon P, Dubois JB,

- Datchary J, et al. Ten-year survival results of a randomized trial of irradiation of internal mammary nodes after mastectomy. *Int J Radiat Oncol Biol Phys* 2013;86:860-6.
9. Nielsen HM, Overgaard M, Grau C, Jensen AR, Overgaard J. Locoregional recurrence after mastectomy in high-risk breast cancer: risk and prognosis: an analysis of patients from the DBCG 82 b&c randomization trials. *Radiother Oncol* 2006;79:147-55.
10. Ragaz J, Olivetto IA, Spinelli JJ, Phillips N, Jackson SM, Wilson KS, et al. Locoregional radiation therapy in patients with high-risk breast cancer receiving adjuvant chemotherapy: 20-year results of the British Columbia randomized trial. *J Natl Cancer Inst* 2005;97:116-26.
11. EBCTCG (Early Breast Cancer Trialists' Collaborative Group), McGale P, Taylor C, Correa C, Cutter D, Duane F, et al. Effect of radiotherapy after mastectomy and axillary surgery on 10-year recurrence and 20-year breast cancer mortality: meta-analysis of individual patient data for 8135 women in 22 randomised trials. *Lancet* 2014;383:2127-35.
12. Tendulkar RD, Rehman S, Shukla ME, Reddy CA, Moore H, Budd GT, et al. Impact of postmastectomy radiation on locoregional recurrence in breast cancer patients with 1-3 positive lymph nodes treated with modern systemic therapy. *Int J Radiat Oncol Biol Phys* 2012;83:e577-81.
13. Kim SI, Cho SH, Lee JS, Moon HG, Noh WC, Youn HJ, et al. Clinical relevance of lymph node ratio in breast cancer patients with one to three positive lymph nodes. *Br J Cancer* 2013;109:1165-71.
14. Chang JS, Lee J, Kim KH, Sohn JH, Kim SI, Park BW, et al. Do recent advances in diagnostic and therapeutic procedures negate the benefit of postmastectomy radiotherapy in N1 patients with a low risk of locoregional recurrence? *Medicine (Baltimore)* 2015;94:e1259.
15. Chang JS, Choi JE, Park MH, Jung SH, Choi BO, Park HS, et al. Trends in the application of postmastectomy radiotherapy for breast cancer with 1 to 3 positive axillary nodes and tumors ≤ 5 cm in the modern treatment era: a retrospective Korean Breast Cancer Society report. *Medicine (Baltimore)* 2016;95:e3592.
16. Park HJ, Shin KH, Kim JH, Ahn SD, Kim JY, Park W, et al. Incorporating risk factors to identify the indication of post-mastectomy radiotherapy in N1 breast cancer treated with optimal systemic therapy: a multicenter analysis in Korea (KROG 14-23). *Cancer Res Treat* 2017;49:739-47.
17. Kunkler IH, Canney P, van Tienhoven G, Russell NS; MRC/EORTC (BIG 2-04) SUPREMO Trial Management Group. Elucidating the role of chest wall irradiation in 'intermediate-risk' breast cancer: the MRC/EORTC SUPREMO trial. *Clin Oncol (R Coll Radiol)* 2008;20:31-4.
18. Han A, Lee KE, Lee HK, Park YH, Kim J, Kim SW, et al. Meeting highlights: the first Korean breast cancer treatment consensus conference. *J Breast Cancer* 2014;17:308-13.
19. Donker M, van Tienhoven G, Straver ME, Meijnen P, van de Velde CJ, Mansel RE, et al. Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer (EORTC 10981-22023 AMAROS): a randomised, multicentre, open-label, phase 3 non-inferiority trial. *Lancet Oncol* 2014;15:1303-10.
20. Giuliano AE, Hunt KK, Ballman KV, Beitsch PD, Whitworth PW, Blumencranz PW, et al. Axillary dissection vs no axillary dissection in women with invasive breast cancer and sentinel node metastasis: a randomized clinical trial. *JAMA* 2011;305:569-75.