Clinical Implication of Triple-Negative Breast Cancer in the Era of Breast-Conserving Therapy

Sanghwa Kim

Department of Medicine

The Graduate School, Yonsei University

Clinical Implication of Triple-Negative Breast Cancer in the Era of Breast-Conserving Therapy

Directed by Professor Seung Il Kim

The Master's Thesis
submitted to the Department of Medicine
the Graduate School of Yonsei University
in partial fulfillment of the requirements for the degree
of Master of Medical Science

Sanghwa Kim

June 2015

This certifies that the Master's Thesis of
Sanghwa Kim is approved.

Thesis Committee Member#1 : Seung Il Kim

Thesis Committee Member#2 : Joo Hyuk Sohn

Thesis Committee Member#3 : Ja Seung Koo

The Graduate School
Yonsei University

June 2015

ACKNOWLEDGEMENTS

I am extremely grateful to all of them help me make this study. By virtue of my professors' guidance, I could finish this work. Thank to my lovely friends. Whenever I don't know what to do for process of the master's degree, their aids are so priceless to me.

And my family, always make me happy, I love you.

<TABLE OF CONTENTS>

LIST OF FIGURES

LIST OF TABLES

ABSTRACT

Clinical Implication of Triple-Negative Breast Cancer in the Era of Breast-Conserving Therapy

Sanghwa Kim

Department of Medicine
The Graduate School, Yonsei University

(Directed by Professor Seung Il Kim)

Background and Objectives

The optimum local surgical strategy regarding Breast-Conserving Therapy (BCT) for Triple-Negative Breast Cancer (TNBC) is controversial. We evaluated the clinical outcomes of BCT in women with TNBC compared to those without TNBC, using a large, single center cohort.

Methods

We performed a retrospective analysis of 1533 women (TNBC n=321; non-TNBC n=1212) who underwent BCT for primary breast cancer between 2000 and 2010. Clinicopathological characteristics, locoregional recurrence-free survival (LRFS), and overall survival (OS) were analyzed.

Results

Tumors from the TNBC group had higher T stage (T2 37.4% vs. 21.0%, $p<0.001$), lower N stage (N0 86.9% vs. 75.5%, $p<0.001$), and higher histologic grade (Grade III 66.8% vs. 15.4%, $p<0.001$) versus the non-TNBC group. There were no differences in 5-year LRFS rates between the TNBC and non-TNBC

groups (98.7% vs. 97.8%, p=0.63). The non-TNBC group showed a slightly better 5-year OS than the TNBC group, but the difference was not significant (96.2% vs. 97.3%, p=0.72). In multivariate analyses, TNBC was not associated with poor clinical outcomes in terms of LRFS and OS (HR for LRFS=0.37, 95% CI=0.10-1.31, HR for OS=1.03, 95% CI=0.31-3.39).

Conclusions

TNBC patients who underwent BCT showed relatively low locoregional recurrence. BCT is an acceptable surgical approach in selected patients with TNBC.

Key words : breast neoplasms, triple-negative breast neoplasms, mastectomy, segmental

Clinical Implication of Triple-Negative Breast Cancer in the Era of Breast-Conserving Therapy

Sanghwa Kim

Department of Medicine
The Graduate School, Yonsei University

(Directed by Professor Seung Il Kim)

I. INTRODUCTION

The use of breast-conserving therapy (BCT) has increased as a definitive surgical treatment for early breast cancer patients; BCT is performed in about 70% of breast cancer operations in Korea.[1] The wide use of BCT is based on previous randomized trials showing favorable survival outcomes of BCT compared to mastectomy.[2-5] For this reason, in 1990, the National Institutes of Health (NIH) Consensus Development Conference on Treatment of Early-Stage Breast Cancer recommended BCT for the majority of women with early-stage breast cancer.[6]

In 2000, Perou et al. determined the molecular subtypes of breast cancer, which were distinguished by the differences in gene expression patterns.[7] Breast cancer subtypes, classified according to the molecular phenotype, show different clinicopathological features, and influence prognosis and response to treatment.[8-12] Currently, immunohistochemistry (IHC)-based molecular classification is used as a surrogate for gene expression profiling.[8-10] Molecular

subtyping based on IHC could provide a standard method for determining the treatment and surveillance strategies in breast cancer patients.[9,11,12]

Among breast cancer subtypes, triple-negative breast cancer (TNBC), in which tumors are negative for estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) expression, has drawn substantial attention because of its aggressive behavior, high risk of early relapse, and poor overall survival.[11,12] There are no proven effective target therapies for the TNBC subtype of breast cancer, making it a clinical challenge for optimal patient management.[13,14] Some studies showed a high risk of local recurrence after BCT in patients who had several clinical risk factors including specific molecular markers or gene expression patterns, such as those exhibited by the TNBC or HER2-enriched subtypes.[15-19] Conversely, other studies have argued that BCT could safely replace mastectomy regardless of the breast cancer subtype.[19-24] Thus, the use of BCT for TNBC is an ongoing concern for surgeons in this era of molecular subtyping for breast cancer. For this reason, we compared the clinical outcome between patients with TNBC and non-TNBC, who underwent BCT to determine the utility of BCT as a treatment for TNBC.

II. METHODS

Patient Cohort

We used the Breast Cancer Registry database of Severance Hospital, Yonsei University Health System to perform a retrospective analysis. The patient cohort consisted of 1533 women who underwent BCT due to primary breast

cancer between 2000 and 2010. Patients who received neoadjuvant chemotherapy, presented with initial distant metastases, or had large size tumors were excluded from the analysis. Patient characteristics including age, T stage, N stage, pathologic type, histologic grade, adjuvant hormone therapy, and adjuvant chemotherapy were reviewed. This study was reviewed and approved by the Institutional Review Board of Severance Hospital, Yonsei University Health System.

Tumor classification

Tumors with <10% ER/PR staining on IHC were considered to be ER/PR negative. We defined HER2-positive tumors as those with 3+ overexpression by immunohistochemical testing (IHC) or HER2 amplification by fluorescence in situ hybridization (FISH). Cases with HER2 expression levels of 0~1+ and 2+ with non-amplification by FISH were considered as HER2-negative. However, we could not confirm HER2 amplification by FISH or silver-enhanced in situ hybridization (SISH) because testing for the HER2 status and approval of the use of trastuzumab were not sanctioned by the Korean National Health Insurance Service for cases prior to the mid- 2000s.

Patient classification

Patients were classified according to the tumor phenotype using the presence or absence of tumor markers by IHC or FISH. TNBC was negative for ER, PR, and HER2 expression, while non-TNBC was defined as least one positive result for ER, PR, or HER2 expression.

The criteria according to the 6th edition of the American Joint Committee on Cancer edition Cancer Staging Manual were used for TNM staging.[25] Adjuvant endocrine therapy, radiation therapy, or adjuvant chemotherapy was administered, if indicated.

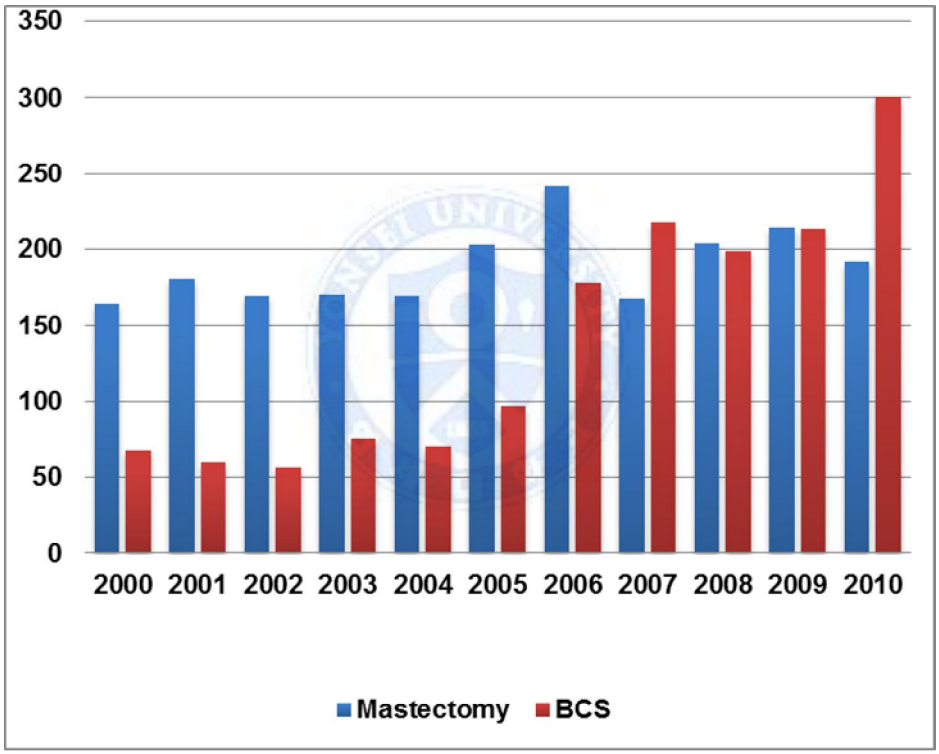

Figure 1. Numbers of mastectomies versus breast-conserving surgeries for T1-2 breast cancer patients in our institiution between 2000 and 2010

Statistical analysis

Categorical variables were analyzed using Chi-square or Fisher's exact test and continuous variables were analyzed by Student's t-test. Locoregional recurrence-free survival (LRFS) was measured from the date of the definitive surgery to the date of the first documented locoregional recurrence. The overall survival (OS) was calculated from the date of the definitive surgery to the date of death. Death without any other identifiable cause was considered in OS analysis. LRFS and OS were plotted using the Kaplan-Meier method and compared using the log-rank test.

Cox proportional hazard models were used for multivariate analyses to determine the association of the TNBC subtype with survival outcomes, after adjusting for potentially confounding variables.

P-values of <0.05 were considered statistically significant; all tests were two-sided. Statistical analyses were carried out using commercially available statistical software (SPSS Statistics 20, IBM, Chicago, IL).

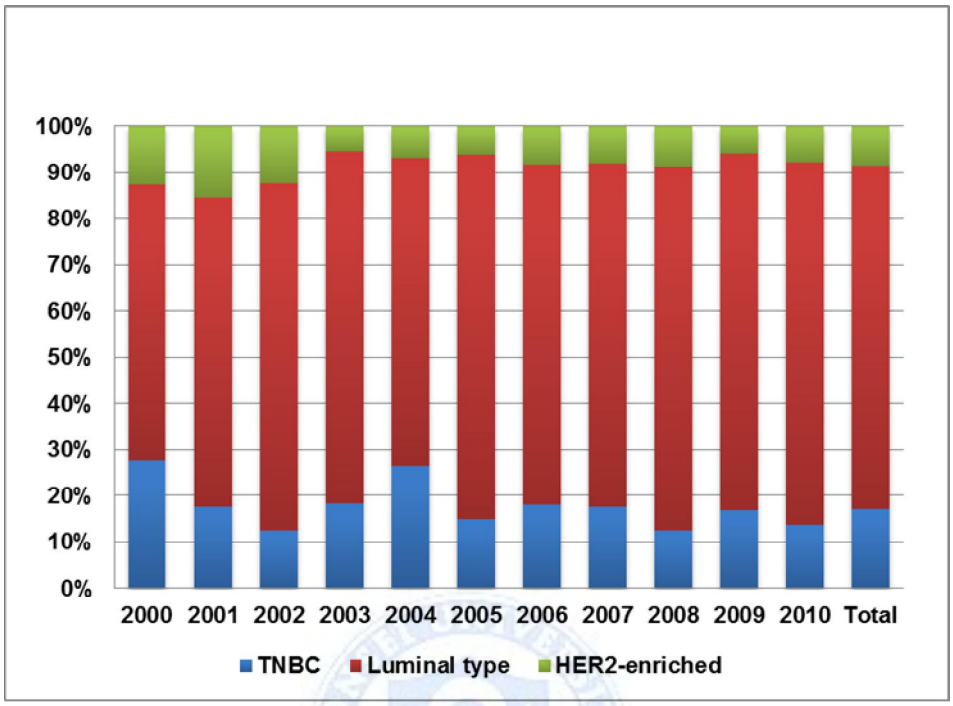

Figure 2. Molecular subtype proportions according to breast cancer subtype with breast conserving therapy

III. RESULTS

Clinicopathological characteristics of the patient groups

The median follow up period of all patients was 57 months (range 0-156).

The number of breast cancer patients who received BCT in our institution increased between 2000 and 2010 (Figure 1). BCT has been performed in half of all breast cancer operations since 2006.

Figure 2 shows the proportion of molecular subtypes in BCT patients during the study period. Since 2000, the proportions of TNBC and non-TNBC breast cancer patients who underwent BCT (~20%) were similar.

Baseline characteristics for the patients and tumor classification according to the subtype are described in Table 1. Of 1533 tumors, 1212 were non-TNBC and 321 were of the TNBC subtype. The mean age of all the patients was 48.7 ± 9.5 years at diagnosis; however, the age distribution was different between the two groups: the TNBC group had more young patients than the non-TNBC group. There were 51 patients (15.9%) younger than 35 years of age in the TNBC group, and 56 patients (4.6%) younger than 35 years of age in the non-TNBC group, respectively ($p<0.001$). The TNBC group had larger tumors (T2 37.4% vs. 21.0%, $p<0.001$), fewer nodal metastases (N0 86.9% vs. 75.5%, $p<0.001$), and tumors with higher histological grade (Grade III 66.8% vs. 15.4%, $p<0.001$) than the non-TNBC group. The patients with TNBC had more tumors with other histological types than the patients with non-TNBC (13.4% vs. 7.4%, $p=0.001$). In the non-TNBC group, approximately one in ten patients (10.7%) had ER-negative tumors, and one quarter of the patients (23.5%) had PR-negative ($p<0.001$) tumors. In addition, tumors from 216 non-TNBC cases were positive for amplification of HER2 (19.5%).

Adjuvant hormone therapy was administered to 1131 patients (93.3%) in the non-TNBC group compared to only 2.8% of patients in the TNBC group. More patients with TNBC received adjuvant chemotherapy than patients with non-TNBC, and this difference was significant (87.9% vs. 60.0%, $p<0.001$).

Table 1. Baseline patient and tumor characteristics

Baseline Characteristics	Non-TNBC (n=1212)		TNBC (n=321)		All patients (n=1533)		p-value*
	n	%	n	%	n	%	
Age							<0.001
≤35	56	4.6%	51	15.9%	107	7.0%	
>35	1156	95.4%	269	84.1%	1425	93.0%	
T stage							<0.001
T1	957	79.0%	201	62.6%	1158	75.5%	
T2	255	21.0%	120	37.4%	375	24.5%	
N stage							<0.001
N0	915	75.5%	279	86.9%	1194	77.9%	
N1	241	19.9%	37	11.5%	278	18.1%	
N2	42	3.5%	5	1.6%	47	3.1%	
N3	14	1.2%	0	0.0%	14	0.9%	
Histological Type							0.001
Ductal	1079	89.0%	274	85.4%	1353	88.3%	
Lobular	43	3.5%	4	1.2%	47	3.1%	
Other	90	7.4%	43	13.4%	133	8.7%	
Histological Grade							<0.001
I	351	31.9%	16	5.7%	367	26.6%	
II	580	52.7%	77	27.5%	657	47.6%	
III	169	15.4%	187	66.8%	356	25.8%	
ER							<0.001
Negative	130	10.7%	321	100.0%	451	29.4%	
Positive	1082	89.3%	0	0.0%	1082	70.6%	
PR							<0.001
Negative	285	23.5%	321	100.0%	606	39.5%	
Positive	927	76.5%	0	0.0%	927	60.5%	
HER2							<0.001
Negative	892	80.5%	321	100.0%	1213	84.9%	
Positive	216	19.5%	0	0.0%	216	15.1%	
Hormone therapy							<0.001
No	81	6.7%	312	97.2%	393	25.6%	
Yes	1131	93.3%	9	2.8%	1140	74.4%	
Adjuvant chemotherapy							<0.001
No	485	40.0%	39	12.1%	524	34.2%	
Yes	726	60.0%	282	87.9%	1008	65.8%	

Abbreviations: TNBC, triple-negative breast cancer; ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2

*Non-TNBC vs. TNBC

Clinical outcomes

Figures 3 and 4 illustrate the Kaplan-Meier plots of LRFS and OS comparing the two groups. Locoregional recurrence developed in seven cases (2.2%) with TNBC and in 28 cases (2.3%) with non-TNBC, which was not significantly different. LRFS for the TNBC group was comparable to the non-TNBC group by log-rank test (5-year LRFS of TNBC vs. non-TNBC: 98.7% vs. 97.8%, p=0.63) (Figure 3). Thirteen patients (4.0%) in the TNBC group and 39 patients (3.2%) in the non-TNBC group died during the follow up period. The non-TNBC group survived slightly longer than the TNBC group until 5 years after surgery, but this difference was not statistically significant (96.2% vs. 97.3%, p=0.72) (Figure 4).

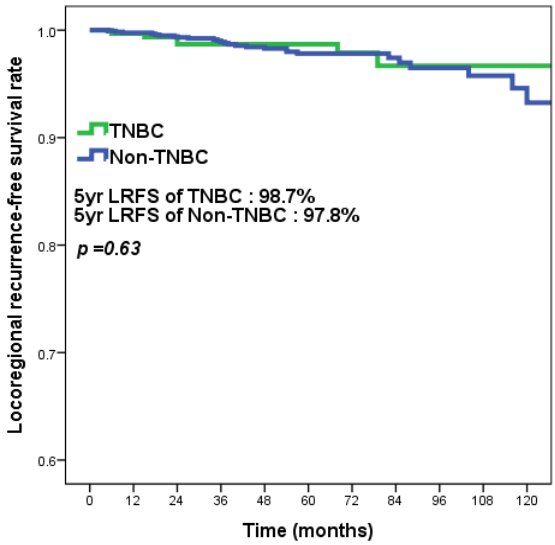

Figure 3. Univariate analysis of locoregional recurrence-free survival after breast-conserving therapy according to TNBC and non-TNBC subtypes

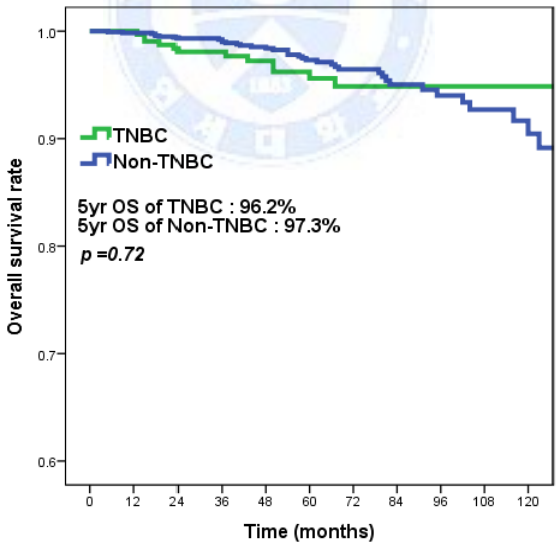

Figure 4. Univariate analysis of overall survival after breast-conserving therapy according to TNBC and non-TNBC subtypes

In multivariable analyses, the TNBC group did not show a significantly increased risk compared to the non-TNBC for locoregional recurrence and death (HR for LRFS =0.37, 95% CI=0.10-1.31, HR for OS=1.03, 95% CI=0.31-3.39) (Table 2). Only nodal stage independently affected the OS, but it was not predictive for the prognosis of LRFS.

Table 2. Multivariate analysis for locoregional recurrence-free survival and overall survival

Multivariate analysis	Locoregional recurrence-free survival				Overall survival			
	Hazard ratio	95% CI		*p*-value	Hazard ratio	95% CI		*p*-value
		Lower	Upper			Lower	Upper	
Subtype								
Non-TNBC	Ref.				Ref.			
TNBC	0.37	0.10	1.31	0.12	1.03	0.31	3.39	0.96
Age								
≤35	Ref.				Ref.			
>35	0.73	0.21	2.53	0.62	0.96	0.34	2.76	0.94
T stage								
T1	Ref.				Ref.			
T2	1.45	0.66	3.21	0.36	1.09	0.58	2.05	0.80
N stage								
N0	Ref.				Ref.			
N+	0.82	0.33	2.03	0.67	2.06	1.08	3.92	0.03
Histological Grade								
I/II	Ref.				Ref.			
III	1.32	0.55	3.17	0.53	1.51	0.75	3.06	0.25
Hormone Therapy								
No	Ref.				Ref.			
Yes	0.45	0.15	1.38	0.16	0.99	0.32	3.06	0.98
Adjuvant chemotherapy								
No	Ref.				Ref.			
Yes	0.72	0.30	1.75	0.47	1.26	0.53	2.99	0.60

IV. DISCUSSION

Based on several randomized-controlled trials, BCT proved to have clinical outcomes equivalent to mastectomy, and has become the standard local treatment option for women with early-stage breast cancer.[2-5] Given the aggressive features of TNBC, however, there is a concern that a more aggressive treatment approach should be considered.[14] The current study demonstrated that clinical outcomes in terms of LRFS and OS in patients with TNBC who underwent BCT were not different from those with non-TNBC.

The use of BCT for breast cancer patients has increased significantly at our institution since 2006. According to the KBCS registry data, while the proportion of patients who underwent total mastectomy decreased from 71.2% in 2000 to 33.8% in 2011, the proportion of patients who underwent BCT surgery increased from 27.9% in 2000 to 65.7% in 2011.[1] These data are concordant with our results.

TNBC generally comprises 10-20% of breast cancers.[26] with a reported prevalence of 12.5% in a large, California population-based study by Bauer et al.[27], in spite of racial differences in the prevalence of TNBC.[10,28] In agreement with these studies, our data showed a 10-20% proportion of TNBC in the breast cancer population, except for two years, 2000 and 2004. Higher numbers of TNBC cases in 2000 and 2004 might reflect inaccurate classification of breast cancer subtypes in those years. Subsequently, the proportions of TNBC and non-TNBC cases in the breast cancer populations were similar through the late

2000s.

The data regarding the rates of locoregional recurrence or distant recurrence rate for TNBC patients with BCT are incongruent. In our study, the LRFS of TNBC and non-TNBC patients was not significantly different, but the OS of TNBC patients was slightly reduced until 6 years after the BCT, which might have been due to the aggressive behavior of TNBC. Interestingly, TNBC patients had a better clinical outcome if they survived longer than 6 years after treatment, compared to non-TNBC patients. After we adjusted for confounding factors in the prognosis, such as age, stage, histologic grade, and systemic therapy, the multivariate analysis revealed that TNBC was unlikely to be an independent prognostic factor affecting the decision to undergo BCT in breast cancer patients. Similarly, Haffty et al. showed no difference in the ipsilateral breast relapse-free survival between the patients with TNBC and other subtypes with conservative management.[24] Patients classified as TNBC were younger and had larger tumors than other subtypes, but had similar LN metastasis rates.[24] The triple-negative subtype was an independent predictor of distant metastasis.[24] In contrast, Arvold et al. showed that the TNBC patients had a significantly increased risk of local recurrence compared with luminal subtypes.[29] In addition, 91% of the patients in that study received adjuvant systemic therapy (but no trastuzumab); the data were stratified according to the luminal subtype by histologic grade; the study compared five breast cancer subtypes and age quartiles, and demonstrated that young age remained an independent risk factor

for locoregional recurrence.[29] A similar study by Nguyen et al. also reported that the breast cancer subtype, as approximated by the ER, PR, and HER-2 status, was significantly associated with both local and distant recurrence after BCT.[18] In that study, Luminal B and HER2-enriched subtypes had more lymph node metastasis and lymphovascular invasion than TNBC, but the TNBC group had larger tumors and received more chemotherapy.[18] Meta-analysis of 22 studies by Wang et al. reported that the TNBC subtype was associated with increased risks of both ipsilateral locoregional recurrence and distant metastasis compared to non-TNBC subtypes.[19] In the TNBC cohort, however, the patients who received BCT were less likely to develop ipsilateral locoregional recurrence and distant metastasis compared to the patients who underwent a mastectomy.[19]

In a previous study that compared the characteristic features of TNBC and other subtypes, the TNBC group was characterized by younger patients, larger and higher grade tumors, and more lymph node metastasis.[14] Our results showed that TNBC patients were younger, had larger tumors with higher histologic grade than non-TNBC patients, and had clinicopathological features that were similar to TNBC patients in prior studies, except for lymph node metastasis. TNBC patients had less metastasis to the lymph nodes and underwent more adjuvant chemotherapy, which might have been responsible for the better outcome of these patients. In addition, the non-TNBC group included an HER2-enriched type, which tended to have more lymph node metastasis than TNBC.[11,18] Dent et al. also showed that TNBC had a more aggressive clinical

course, but this feature was transient. The peak time to recurrence in TNBC is 2-3 years and thereafter, the recurrence rate of TNBC is similar to other subtypes.[14] These features of TNBC could support our result, which showed favorable outcomes for TNBC compared to non-TNBC after BCT.

However, there were limitations to the retrospective study design. First, because trastuzumab was approved for use by the Korean National Health Insurance beginning in the middle 2000s, testing for HER2 expression and prescribing trastuzumab were not routinely performed. Thus, there was a lack of information about the administration of trastuzumab or HER2 evaluations in the registry prior to that time. Second, some TNBC patients received hormone therapy. In the current study, about 2.8% of TNBC patients were treated with hormone therapy, and their tumors were weakly positive for hormone receptor expression (1~9%) on IHC. The tumors with weak hormone receptor positivity were regarded as negative., Whether hormone receptor positivity of 1-9% in these patients was real or an artifact was in dispute among many physicians.[30] In our institution, hormone receptor expression over 1% was considered as positive according to the guidelines from the American Society of Clinical Oncology and the College of American Pathologists in 2010, which recommended a threshold of 1% or more for classifying a breast cancer as ER-positive.[31] Changes in the definition of threshold of hormone receptor expression can influence clinical outcomes. The complexity of clinical, biological, and histopathological information about breast cancer creates

difficulties for managing locoregional disease. Moreover, there are no specific locoregional treatment guidelines for TNBC.[32]

V. CONCLUSION

Given that the current study showed relatively low locoregional recurrence in the patients with early TNBC and comparable outcomes between TNBC and non-TNBC, BCT may be an acceptable surgical approach in selected patients with TNBC.

REFERENCES

1. Kim Z, Min SY, Yoon CS, Lee HJ, Lee JS, Youn HJ, et al. The basic facts of korean breast cancer in 2011: results of a nationwide survey and breast cancer registry database. J Breast Cancer 2014;17:99-106.
2. Veronesi U, Cascinelli N, Mariani L, Greco M, Saccozzi R, Luini A, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. N Engl J Med 2002;347:1227-32.
3. van Dongen JA, Voogd AC, Fentiman IS, Legrand C, Sylvester RJ, Tong D, et al. Long-term results of a randomized trial comparing breast-conserving therapy with mastectomy: European Organization for Research and Treatment of Cancer 10801 trial. J Natl Cancer Inst 2000;92:1143-50.
4. Poggi MM, Danforth DN, Sciuto LC, Smith SL, Steinberg SM, Liewehr DJ, et al. Eighteen-year results in the treatment of early breast carcinoma with mastectomy versus breast conservation therapy: the National Cancer Institute Randomized Trial. Cancer 2003;98:697-702.
5. Fisher B, Anderson S, Bryant J, Margolese RG, Deutsch M, Fisher ER, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. N Engl J Med 2002;347:1233-41.
6. NIH consensus conference. Treatment of early-stage breast cancer. JAMA 1991;265:391-5.
7. Perou CM, Sorlie T, Eisen MB, van de Rijn M, Jeffrey SS, Rees CA, et al. Molecular portraits of human breast tumours. Nature 2000;406:747-52.
8. Brenton JD, Carey LA, Ahmed AA, Caldas C. Molecular classification and molecular forecasting of breast cancer: ready for clinical application? J Clin Oncol 2005;23:7350-60.

9. Tang P, Skinner KA, Hicks DG. Molecular classification of breast carcinomas by immunohistochemical analysis: are we ready? Diagn Mol Pathol 2009;18:125-32.
10. Carey LA, Perou CM, Livasy CA, Dressler LG, Cowan D, Conway K, et al. Race, breast cancer subtypes, and survival in the Carolina Breast Cancer Study. JAMA 2006;295:2492-502.
11. Park S, Koo JS, Kim MS, Park HS, Lee JS, Lee JS, et al. Characteristics and outcomes according to molecular subtypes of breast cancer as classified by a panel of four biomarkers using immunohistochemistry. Breast 2012;21:50-7.
12. Voduc KD, Cheang MC, Tyldesley S, Gelmon K, Nielsen TO, Kennecke H. Breast cancer subtypes and the risk of local and regional relapse. J Clin Oncol 2010;28:1684-91.
13. Chen X, Yu X, Chen J, Zhang Z, Tuan J, Shao Z, et al. Analysis in early stage triple-negative breast cancer treated with mastectomy without adjuvant radiotherapy: patterns of failure and prognostic factors. Cancer 2013;119:2366-74.
14. Dent R, Trudeau M, Pritchard KI, Hanna WM, Kahn HK, Sawka CA, et al. Triple-negative breast cancer: clinical features and patterns of recurrence. Clin Cancer Res 2007;13:4429-34.
15. Harissis HV, Ziogas D, Baltogiannis G. Mastectomy vs breast-conserving surgery: an old dilemma comes again for early breast cancer. Ann Surg Oncol 2010;17:1966-7.
16. Kreike B, Halfwerk H, Armstrong N, Bult P, Foekens JA, Veltkamp SC, et al. Local recurrence after breast-conserving therapy in relation to gene expression patterns in a large series of patients. Clin Cancer Res 2009;15:4181-90.
17. Zaky SS, Lund M, May KA, Godette KD, Beitler JJ, Holmes LR, et al. The negative effect of triple-negative breast cancer on outcome after

breast-conserving therapy. Ann Surg Oncol 2011;18:2858-65.

18. Nguyen PL, Taghian AG, Katz MS, Niemierko A, Abi Raad RF, Boon WL, et al. Breast cancer subtype approximated by estrogen receptor, progesterone receptor, and HER-2 is associated with local and distant recurrence after breast-conserving therapy. J Clin Oncol 2008;26:2373-8.

19. Wang J, Xie X, Wang X, Tang J, Pan Q, Zhang Y, et al. Locoregional and distant recurrences after breast conserving therapy in patients with triple-negative breast cancer: a meta-analysis. Surg Oncol 2013;22:247-55.

20. Zumsteg ZS, Morrow M, Arnold B, Zheng J, Zhang Z, Robson M, et al. Breast-conserving therapy achieves locoregional outcomes comparable to mastectomy in women with T1-2N0 triple-negative breast cancer. Ann Surg Oncol 2013;20:3469-76.

21. Bhatti AB, Khan AI, Siddiqui N, Muzaffar N, Syed AA, Shah MA, et al. Outcomes of triple-negative versus non-triple-negative breast cancers managed with breast-conserving therapy. Asian Pac J Cancer Prev 2014;15:2577-81.

22. Gangi A, Chung A, Mirocha J, Liou DZ, Leong T, Giuliano AE. Breast-conserving therapy for triple-negative breast cancer. JAMA Surg 2014;149:252-8.

23. Abdulkarim BS, Cuartero J, Hanson J, Deschenes J, Lesniak D, Sabri S. Increased risk of locoregional recurrence for women with T1-2N0 triple-negative breast cancer treated with modified radical mastectomy without adjuvant radiation therapy compared with breast-conserving therapy. J Clin Oncol 2011;29:2852-8.

24. Haffty BG, Yang Q, Reiss M, Kearney T, Higgins SA, Weidhaas J, et al. Locoregional relapse and distant metastasis in conservatively managed triple negative early-stage breast cancer. J Clin Oncol 2006;24:5652-7.

25. Singletary SE, Connolly JL. Breast cancer staging: working with the sixth edition of the AJCC Cancer Staging Manual. CA Cancer J Clin 2006;56:37-47; quiz 50-1.
26. Boyle P. Triple-negative breast cancer: epidemiological considerations and recommendations. Ann Oncol 2012;23 Suppl 6:vi7-12.
27. Bauer KR, Brown M, Cress RD, Parise CA, Caggiano V. Descriptive analysis of estrogen receptor (ER)-negative, progesterone receptor (PR)-negative, and HER2-negative invasive breast cancer, the so-called triple-negative phenotype: a population-based study from the California cancer Registry. Cancer 2007;109:1721-8.
28. Ismail-Khan R, Bui MM. A review of triple-negative breast cancer. Cancer Control 2010;17:173-6.
29. Arvold ND, Taghian AG, Niemierko A, Abi Raad RF, Sreedhara M, Nguyen PL, et al. Age, breast cancer subtype approximation, and local recurrence after breast-conserving therapy. J Clin Oncol 2011;29:3885-91.
30. Yi M, Huo L, Koenig KB, Mittendorf EA, Meric-Bernstam F, Kuerer HM, et al. Which threshold for ER positivity? a retrospective study based on 9639 patients. Ann Oncol 2014;25:1004-11.
31. Hammond ME, Hayes DF, Dowsett M, Allred DC, Hagerty KL, Badve S, et al. American Society of Clinical Oncology/College Of American Pathologists guideline recommendations for immunohistochemical testing of estrogen and progesterone receptors in breast cancer. J Clin Oncol 2010;28:2784-95.
32. Moran MS. Should Triple-Negative Breast Cancer (TNBC) Subtype Affect Local-Regional Therapy Decision Making? Am Soc Clin Oncol Educ Book 2014;34:e32-6.

ABSTRACT(IN KOREAN)

유방보존술을 시행한 유방암환자에서 삼중음성유방암의 임상적 영향

<지도교수 김승일>

연세대학교 대학원 의학과

김상화

삼중음성유방암 환자는 재발률이 높고, 예후가 안 좋으므로 이들에게 유방보존술이 적합한 수술 방법인지에 대해서 논란이 되어 왔다. 이 연구에서 유방보존술을 시행받은 삼중음성유방암과 그 외의 유방암 환자의 임상적 예후를 비교하여 유방보존술이 삼중음성유방암에 적합한지 확인하고자 하였다. 이 연구에서는 2000에서 2010년까지 유방암으로 유방보존술을 시행받은 1533명의 환자 (삼중음성유방암 321명, 비삼중음성유방암 1212명) 를 후향적으로 분석하였다. 그 결과, 삼중음성유방암과 비 삼중음성유방암 환자 집단 간에 5년 국소지역재발 무병생존율에 거의 차이가 없었으며 (98.7% vs. 97.8%, p=0.63), 비삼중음성유방암 환자 집단의 5년 전체 생존율이 삼중음성유방암 집단보다 약간 높았으나, 의미있는 결과는 아니었다 (96.2% vs. 97.3%, p=0.72). 결론적으로, 유방보존술을 시행받은 삼중음성유방암 환자에서 낮은 국소지역재발을 보였으며, 적절하게 선택된 삼중음성유방암 환자에게는 유방보존술이 수술적 처치로서 고려해 볼 수 있을 것으로 생각된다.

핵심되는 말 : 유방암, 삼중음성유방암, 유방보존술