The Breast 23 (2014) 586–590

Contents lists available at ScienceDirect

The Breast

journal homepage: www.elsevier.com/brst

Original article

Excision alone for small size ductal carcinoma in situ of the breast

Haeyoung Kim [a, 1], Jae Myoung Noh [b, 1], Doo Ho Choi [b, *], Jihye Lee [c], Seok Jin Nam [d], Jeong Eon Lee [d], Won Park [c], Seung Jae Huh [c]

[a] Department of Radiation Oncology, Hallym University Dongtan Sacred Heart Hospital, South Korea
[b] Department of Radiation Oncology, Samsung Medical Center, Sungkyunkwan University School of Medicine, 50 Irwon-dong, Gangnam-gu, Seoul 135-710, South Korea
[c] Department of Radiation Oncology, Ewha Womans University Medical Center, South Korea
[d] Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, South Korea

ARTICLE INFO

Article history:
Received 31 December 2013
Received in revised form
31 March 2014
Accepted 24 May 2014
Available online 23 June 2014

Keywords:
Intraductal carcinoma
Breast
Surgery
Radiotherapy

ABSTRACT

This study was performed to determine the risk of tumor recurrence after local excision alone in patients with small size (≤1 cm) ductal carcinoma in situ (DCIS) of the breast. We have treated 107 patients who had DCIS measuring ≤1 cm with margin widths of ≥0.3 cm with excision alone per institutional protocol. With a median follow-up time of 58 months, 4 patients developed ipsilateral breast tumor recurrence (IBTR). Two of the 4 recurrences were invasive, whereas 2 were DCIS. The 5-year rate of IBTR was 6.1%. The patients with resection margin of <1.0 cm had significantly higher rate of IBTR than the patients with resection margin of ≥1.0 cm (23.1% vs. 1.5% at 5-year, $p < 0.01$). In conclusion, radiotherapy is necessary in the patients with resection margin of <1.0 cm after excision alone because of the substantial risk of IBTR.

Introduction

Ductal carcinoma in-situ (DCIS) of the breast is a broad-spectrum disease that presents proliferation of epithelial cells within the mammary ducts without invading basement membranes [1]. Even if the lesion of DCIS resides within the ductal system at the initial presentation, there is a chance of an invasion into adjacent stroma [2]. Because DCIS is considered as a precursor to invasive breast cancer, it is important for patients with DCIS to remove the lesion itself and prevent the development of invasive cancer.

As breast-conserving surgery (BCS) combined with radiotherapy is proven successful for invasive breast cancer, the therapeutic approach has been adopted for DCIS. The combination of radiotherapy and breast-conserving surgery has been found to reduce local recurrence by approximately 40%–60% in patients with DCIS [3–6]. Nonetheless, the level of beneficial effects of radiotherapy varies among subgroups of patients [7]. Furthermore, some retrospective studies found that the local tumor control rate after surgery alone was similar to that after surgery followed by radiotherapy in patients with a small lesion at a large resection margin [8–10]. Based on such results, there have been trials of omitting radiotherapy in patients with favorable DCIS who are thought to be at low risk of recurrence after surgery alone [11–13]. Nonetheless, the treatments for DCIS have not been individualized by subsets of tumors. In particular, subgroups of patients who can achieve tumor control by surgical resection alone in the absence of breast irradiation have not been well-defined. As an institutional protocol, we have treated patients with DCIS measuring ≤1 cm with microscopic margin widths of ≥0.3 cm with surgery alone. In the current study, we retrospectively reviewed our results of planned-surgery alone without adjuvant radiotherapy in patients with small DCIS (size of ≤1 cm).

Materials and methods

Patients and treatments

A total of 498 female patients with DCIS received BCS at Samsung Medical Center between December 1999 and December 2009. Among them, 107 patients who had DCIS measuring ≤1 cm with microscopic margin widths of ≥0.3 cm were treated with excision alone without adjuvant radiotherapy per institutional protocol. Seven patients who had resection margin less than 0.3 cm at the side of chest wall were permitted to omit radiotherapy because

* Corresponding author. Tel.: +82 2 3410 2436; fax: +82 2 3410 2619.
E-mail address: doho.choi@samsung.com (D.H. Choi).
[1] Haeyoung Kim and Jae Myoung Noh equally contributed to this work.

http://dx.doi.org/10.1016/j.breast.2014.05.025
0960-9776/

further resection was not possible due to the fascia of the chest wall. The size of pathologic tumors was determined by measuring largest single diameter of DCIS. Margin width was determined with distance between the edge of the tumor and an inked line delineating the margin of normal tissue by direct measurement. We included nine patients who had ultrasound-guided vacuum-assisted biopsy at other institutions for DCIS ≤1 cm. There was no residual tumor on their surgical specimens after BCS that was performed in our hospital. The margin width of tumor was defined as the size of tissues removed by surgery. The hormone receptor status of tumor was evaluated in 83.2% of the patients. Allred scores ranging from 3 to 8 were defined as positive immunoreactivity for ER and PR. HER-2 status was determined by immunohistochemical staining. All patients were treated with wide excision and 23 patients underwent axillary sentinel lymph node biopsy. Tamoxifen was prescribed for 5 years to 83.2% of patients according to physician's opinion. Patient and tumor characteristics are listed in Table 1. The patients were followed up with history taking and physical examination every 6 months and mammography annually. Tumor recurrence was diagnosed with biopsy. All patients gave informed consents.

Statistical analysis

The recurrence-free survival was defined as the interval between surgery to tumor recurrence, and it was calculated using the Kaplan–Meier method. The log-rank test was used to compare the recurrence-free survival between the groups with different variables. Statistical significance was calculated at the 95% confidence interval (p-value <0.05), and all the analyses were performed using the SPSS package (SPSS 12.0 for windows, SPSS Inc, Chicago, IL, USA).

Table 1
Patient's characteristics.

Characteristics		Number	(%)
Age, years			
Median, (Range)	46 (23–80)		
	<40	23	21.5
	≥40	84	78.5
Family history of breast or ovarian cancer	Absent	94	87.9
	Present	13	12.5
Use of tamoxifen	No	18	16.8
	Yes	89	83.2
Hormone receptor of tumor	ER+ and/or PR+/HER2+,−	86	80.4
	ER−/PR−/HER2+	1	0.9
	ER−/PR−/HER2-	2	1.9
	Unknown	18	16.8
Lesion size, cm	<0.5	50	46.7
	≥0.5, ≤1.0	57	53.3
Margin size, cm	<0.3[a]	7	6.5
	≥0.3, <1.0	17	15.9
	≥1.0	83	77.6
Nuclear grade	Low	69	64.5
	Intermediate	30	28.0
	High	8	7.5
Necrosis	Absent	61	57.0
	Present	29	27.1
	Unknown	17	15.9
Architecture	Cribriform	37	34.6
	Solid	18	16.8
	Micropapillary	10	9.3
	Comedo	8	7.5
	Mixed	14	13.1
	Unknown	20	18.7

[a] Tumors with resection margin width less than 0.3 cm were treated with surgery alone if the tumors were located within 0.3 cm of chest wall fascia and further resections were not possible due to the limiting structure in according to surgeon's opinion.

Results

Median follow-up time was 58 months (range, 18–136 months). Ipsilateral breast tumor recurrence (IBTR) was detected in 4 patients while one patient showed recurrent DCIS in the contralateral breast (Table 2). The interval between surgery and recurrence ranged from 36 to 82 months. Among the patients with IBTR, 2 patients developed invasive ductal carcinoma whereas 2 patients showed DCIS. Two of the 4 patients had IBTR adjacent to the initial lumpectomy cavity and 2 had recurrence away from the initial surgical cavity.

Of the patients who developed IBTR, one patient had neurofibromatosis type I (NF-1), which was diagnosed by clinical manifestation along with genetic analysis before the treatment of breast cancer. Genetic tests for BRCA1 and 2 mutations were conducted on the patient who has the family history of breast cancer by her grandmother. She tested negative for BRCA1 and 2 mutations. The patient developed invasive carcinoma at different quadrant of the breast 36 months after initial surgery for DCIS.

The rate of IBTR at 5-year and 10-year were both 6.1% (Fig. 1). The prognostic factors for IBTR were described in Table 3. The patients with resection margin of <1.0 cm had significantly higher rate of IBTR than the patients with resection margin of ≥1.0 cm (23.1% vs. 1.5% at 5-year, $p < 0.01$) (Fig. 2).

Discussion

We observed excellent local control after excision alone in small size DCIS when it was resected with wide margin. Such tumors could be treated with surgery alone without radiotherapy. However, there were frequent local recurrences when the tumors were excised with narrow margin without addition of postoperative radiotherapy. Therefore, for the patients with DCIS which has been resected with close margin, radiotherapy should follow surgery even if the tumor is smaller than 1 cm.

The effect of adjuvant radiotherapy for patients with DCIS in terms of reduction of local recurrence has been demonstrated in several randomized trials [3–6]. In these trials, all subgroups of patients treated with breast conserving surgery were benefitted by radiotherapy. Nonetheless, there has been a clinical hypothesis that there might be subsets of DCIS that can be successfully treated with surgery alone without adjuvant radiotherapy. Three prospective trials and some retrospective studies have evaluated the possibility of omitting adjuvant radiotherapy in patients with DCIS whose risk of recurrence after surgery alone were deemed sufficiently-low (Table 4) [12–16].

In the first of the three prospective trials of surgery alone for DCIS, selected patients by mammographic tumor size and pathologic tumor grade were treated with wide excision with margins of ≥1 cm without adjuvant radiotherapy. The authors included DCIS of grade 1 or 2 with a mammographic extent of ≤2.5 cm [14]. After the median follow-up time of 40 months, 13 out of 158 patients developed local recurrence as the first failure, resulting in 5-year recurrence rate of 12%. According to such a high rate of local relapse after excision alone, the study concluded that adjuvant radiotherapy should be provided to patients with DCIS despite the small tumor sizes and the larger resection margin than 1 cm.

Besides, the Eastern Cooperative Oncology Group (ECOG) performed a prospective observational study on omission of radiotherapy in patients with DCIS [12]. In its trial, patient eligibility was determined by pathologic tumor size, histologic grade, and microscopic margin widths of tumor. Patients with low or intermediate grade DCIS measuring ≤2.5 cm, or high grade DCIS measuring ≤1 cm with margin widths of ≥0.3 cm were included in