: 63 4 Vol. 63, No. 4, October, 2002

, 1

Micrometastases in the Sentinel Lymph Nodes of Patients with Ductal Carcinoma In-Situ of the Breast

Jeong-Han Kim, MD., Jeong-Yoon Song, MD., Suk-Jin Nam, MD., Young-Hyeh Ko, MD. and Jung-Hyun Yang, MD.

Purpose: Although the axillary lymph node (LN) status is the most important prognostic indicator in breast cancer, due to the very low rae of axillary metastasis, the need for an axillary lymph node dissection in ductal carcinoma in situ (DCIS) and DCIS with a microinvasion (DCIS-M) is still controversial. The sentinel lymph node procedure has emerged as a potential alternative to avoid unnecessary axillary lymph node dissection. This study was performed in order to compare the frequency of metastasis in the sentinel node analyzed by various techniques, and the lymph nodes obtained by a routine axillary dissection in patients with DCIS and DCIS-M

Methods: A total of 207 patients who underwent surgery for DCIS and DCIS-M at the Samsung Medical Center between 1994 and 2001, including 27 patients who underwent a sentinel node biopsy, were enrolled in this study. The sentinel node was serially cut into 20 slides per paraffin block of which 3 slides were immunostained with anti-cytokeratin antibodies. The medical records for the clinical, radiological, and pathological findings were reviewed.

Results: The patients were 205 women and 2 men with a mean age of 47 years. The patients presented with a palpable mass (50.2%), abnormal radiological findings detected in a routine check-up (35.7%), nipple discharge (10.1%), and others (3.9%). The operations applied were a total mastectomy in 120 patients, a lumpectomy in 50, and a lumpectomy with an axillary dissection in 31. The histological types of

tumors were DCIS (77.3%) and DCIS with a microinvasion (22.7%). While the conventional pathologic examination showed axillary metastasis in 2 of 151 patients (1.3%) with an axillary dissection, serial sectioning and immunohistochemical staining for cytokeratin on the sentinel node in 27 patients revealed 2 more patients with a micrometastasis that were found to be negative in a conventional pathological examination.

Conclusion: The serial sectioning and immunohistochemical method for the sentinel LNs of patients with DCIS and DCIS-M are superior to a conventional histological examination for detecting a metastatic carcinoma. The patients with a micrometastasis might be considered as a high risk group and a close long-term follow up would be required to define their prognostic significance. (J Korean Surg Soc 2002;63: 276-282)

Key Words: Breast cacner, Mcrometastasis, Sentinel node:

Departments of Surgery and ¹Pathology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

20

7 (ductal carcinoma in situ)

with microinvasion)

.(I)

7 7

: , 50 © 135-710, Tel: 02-3410-3463, Fax: 02-3410-3019 E-mail: jhyang @smc.smsung.co.kr : 2002 2 4 , : 2002 5 25 2001

277 :

27

1,935

22.2%, 50 가

10.1%,

Percent (%)

4.8

22.2

38.6

19.3

13.0

1.9

0.1

99.9

2 (0.1%)

가

47

. Isosulfan blue dye .(3) 3) 9 31% 가 .(3) 28 cytokeratin 34 4 µm 20 3 anti-cytokeratin (AE1+AE3) antibody (Zymed , USA) 가 가 17 1) cytokeratin 10.7% 160 (77.3%) (22.7%)2) 1) 20 70 40 가가 38.6% 1994 11 2001 6 19.3% . 207 (Table 1). 207 3) 2) 가 50.2% 35.7%, 207 28 3.9% (Table 2). isosulfan blue 22 99m Tc-Antimony sulfide 6 isosulfan blue . Isosulfan blue colloid Table 1. Age and sex of patients with DCIS* and DCIS-M[†] 5 cc 가 dye 4 5 10 No. of patients 2 3 cm 가 29 10 Age (years) 20 . 99m Tc-Antimony sulfide colloid 30 39 46 0.5 mCi 2 3 4 40 49 80 50 59 40 27 60 69 (Neoprobe 1500, Neoprobe corperation, USA) 70 4 가 iso-2 Sex sulfan bule dye Male Female 205 . isosulfan blue dye

2

^{*}Ductal carcinoma in-situ; † ductal carcinoma in-situ with microinvarion.

Table	2.	Presenting	symptoms	and	sions
Laule	4.	TICSCHUIIE	SVIIIDIOIIIS	anu	2115

	No. of patients	Percent (%)
Palpable mass	104	50.2
Abnormality on screening exam	74	35.7
Nipple discharge	21	10.1
Others	8	3.9

Table 3. Preoperative diagnostic methods

	No. of patients	Percent (%)
Excisional biopsy	45	26.8
Sono-guided core biopsy	36	21.6
Needle localization	34	20.4
Stereotactic core biopsy	20	12.0
Fine needle aspiration cytology	17	10.2
Incisional biopsy	11	6.6
ABBI*	4	2.4
Total	207	100

 $[*]Advanced\ breast\ biopsy\ instrumentation.$

4)

6)

167
(ex-
(sono-guided
(needle localization) 34,
actic core biopsy) 20 ,
(incisional biopsy) 11 , ABBI (Ad-
umentation) 4 .
가
(Table 3).
179
32.4%
11 가 (Table 4).
(

120 lumpectomy 56 , lumpectomy 31 (Table 5).

Table 4. Mammographic findings

Findings	No. of patients	Percent (%)	
Mass lesion	58	32.4	
Spiculated mass	9	5.0	
Mass density	21	11.7	
Mass with calcification	28	15.7	
Calcification only	110	61.5	
Benign	12	6.7	
Indeterminate	14	7.9	
Malignant	84	46.9	
No abnormality	11	6.1	
Total	179	100	

Table 5. Operative methods

	No. of patients	Percent (%)
Total mastectomy	120	60.0
Lumpectomy	56	27.0
Lumpectomy with ALND*	31	15.0

^{*}Axillary lymph node dissection.

7)

198 (micro focus) 가 14.1% , 3 cm 15.7% 0.1 207 cm 2.02 cm 22.7% 가 . 1 15 1 2 (1.3%)가 1 (phyllodes tumor)

> 28 1 가 11 가

279

Table	6.	Patho!	logic	findings

	N*		No. of patients	Percent (%)
Size (cm)	198	microfocus	28	14.1
		1.0	44	22.2
		1.1 2.0	56	28.3
		2.1 3.0	39	19.7
		3.1	31	15.7
Microinvasion	207	yes	47	22.7
		no	160	
L/N metastasis	151	yes	2	1.3
		no	149	
Comedo pathology	160	yes	79	49.4
		no	81	
Multicentricity	197	yes	26	13.2
		no	12 1	
Estrogen receptor	15 1	Positive	109	72.2
		Negative	42	
Progesterone receptor	15 1	Positive	92	60.9
_		Negative	59	

^{*}Number of patients with available data.

Table 7. Detection of micrometastases by serial sectioning and immunohistochemical study for sentinel lymph nodes

		No. of patients
Serial section	Positive	1
	Negative	26
IHC* with cytokeratin	Positive	2^{\dagger}
(AE l/AE3)	Negative	25

^{*}Immunohistochemical staining; † 1 case detected by serial section was detected also by IHC staining.

. 7

9) cytokeratin

Fig. 1. Micrometastasis detected by IHC staining with cytokeratin. Note a few cells in the subcapsular sinus.

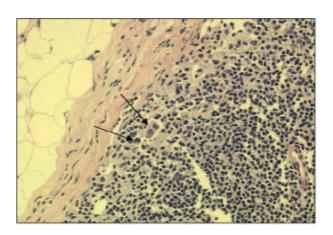


Fig. 2. H&E staining following serial section. A few tumor cells can be seen at the nearby slide.

28 1.3) 1 27 34 (1 cytokeratin (AE1, AE3)

280	: 63	4 2002					
가 1 mm	1997 .(4)	AJCC	T lmic	10%	10	.(10)	4%
		2 4%	.(5)			. 2	40
15 7 .(8) 7	22% 851 (7)	(6) 7} 101 (11.9%) ⁷	71	31% 207	58% (7)	.(6) 73.2%	,
10.7%			가	가 가			
가			가	National St B-17 protocol 8	urgical Adjuva		t (NSABP) impectomy 13%
(9)		·		가		31%	.(11)
178 81.2%가	30%	(needle	localization)	(comedo n	ecrosis)		
core biopsy), instrumentation)	, 가	ABBI (Advanced l	7 35.7% (stereotactic breast biopsy	가 Silverstein(12) Organization for Cancer tocol 10853(13) 가		가 otocol B-17 Treatment (EC	European PRTC) pro-
. (ove	フト r-treatment)	? }			가 가		lump-
	가			ectomy .	3	가 가	

: 281

```
9 (12%),
                                                                                         76
                      가
                                                  25%
                                                                       31
                                                                                3 (10%)
                                                   가
                           .(14)
                                                                   Pendas
                                                                            (19)
                                                                                     87
                                                                                             5 (6%)
            가
                                          가
    .(12)
                                                                                       27
                                                                                                      , cytokeratin (AE1
                                                                                               1
                                                              +AE3)
                                                                                                             2 (7.1%)
                 cytokeratin
                                                                                               1
                                                                                                     cytokeratin
              가
                                                                                     , cytokeratin
                   736
                                              cytokeratin
20%
                            가
                                                                                 가
                                                                                           2
                                                                                                1
                                              가
           .(15)
                                                                      , 1
                                                                             Klauber-DeMore
                                                                                               (18)
              가
              . Fisher
                       (16)
                             814
                                                                                                   . Anderson(20)
        7.5
                                1.8%
                                                , 1.8%
                                  , Silverstein(12) 6.9
                                                                   가
     879
0.9%, 0.6%
                                                                 scrubbing
                                                                                     가
                                                                                                가
                                                                   Linden
                                                                           Zarbo(21)
                                          가
                                                    가
                                                                                         가 cytokeratin
                         가
                                                                                                                10%
                                                                                                   cytokeratin
                                                                                        (interstitial reticular cell)
               207
                                                     15 1
                                                                                                    Silverstein(12)
                                                Frykberg
                                                                                 가
             2 (1.3%)
   Bland(17)
              5%
                                                                                                                    가
                                                                                   207
               . Klauber-DeMore
                                 (18)
                                             , 2)
                                                                   27
                            , 3)
                                                  , 5)
                                                                                                                2
             , 4)
                                                                              가
                                                                                  가
                                                                                           가
   cytokeratin
```

cytokeratin

가

가 가

REFERENCES

- Greenlee RT, Murray T, Bolden S, Wingo PA. Cancer statistics. 2000. CA Cancer J Clin 2000:50:7-33.
- Silverstein MJ, Rosser RJ, Gierson ED, Waisman JR, Gamagami P, Hoffman RS, et al. Axillary lymph node dissection for intraductal breast carcinoma--is it indicated? Cancer 1987; 59:1819-24.
- Klauber-Demore N, Tan LK, Liberman L, Kaptain S, Fey J, Borgen P, et al. Sentinel lymph node biopsy: is it indicated in patients with high-risk ductal carcinoma-in-situ and ductal carcinoma-in-situ with microinvasion. Ann Surg Oncol 2000;7: 636-42.
- American Joint Committee on Cancer. Manual for Staging of Cancer. 5th ed. Philadelphia (PA): Lippincott-Raven Publisher; 1997. p. 171.
- 5) Silverstein MJ, Lagios MD, Craig PH, Waisman JR, Lewinsky BS, Colburn WJ, et al. A prognostic index for ductal carcinoma in situ of the breast. Cancer 1996;77:2267-74.
- 6) Cox CE, Nguyen K, Gray RJ, Salud C, Ku NN, Dupont E, et al. Importance of lymphatic mapping in ductal carcinoma in situ (DCIS): why map DCIS? Am Surg 2001;67:513-9.
- Lee HD, Kim DY, Choi JW, Park BW, Jung WH, Oh KK. Clinicopathological analysis of ductal carcinoma in situ (DCIS) and ductal carcinoma in situ with microinvasion. J Korean Surg Soc 2001;60:495-500.
- 8) Simon MS, Lemanne D, Schwartz AG, Martino S, Swanson GM. Recent trends in the incidence of in situ and invasive breast cancer in the Detroit metropolitan area (1975-1988). Cancer 1993;71:769-74.
- Park HL, Suh JM, Lee SD, Noh SI, Nam SJ, Yang JH. The role of a needle localization breast biopsy for the diagnosis of nonpalpable breast cancer. J Korean Surg Soc 2000;59:321-8.
- Sakorafas GH, Tsiotou AG. Ductal carcinoma in situ (DCIS) of the breast: evolving perspectives. Cancer Treat Rev 2000;

- 26:103-25.
- 11) Fisher ER, Dignam J, Tan-Chiu E, Costantino J, Fisher B, Paik S, et al. Pathologic findings from the National Surgical Adjuvant Breast Project (NSABP) eight-year update of Protocol B-17: intraductal carcinoma. Cancer 1999:86:429-38.
- 12) Silverstein MJ, Parker R, Grotting JC, Cote RJ, Russell CA. Ductal carcinoma in situ (DCIS) of the breast: diagnostic and therapeutic controversies. J Am Coll Surg 2001;192:196-214.
- 13) Julien JP, Bijker N, Fentiman IS, Peterse JL, Delledonne V, Rouanet P, et al. Radiotherapy in breast-conserving treatment for ductal carcinoma in situ: first results of the EORTC randomised phase III trial 10853. EORTC Breast Cancer Cooperative Group and EORTC Radiotherapy Group. Lancet 2000; 355:528-33.
- 14) Fisher B, Bauer M, Wickerham DL, Redmond CK, Fisher ER, Cruz AB, et al. Relation of number of positive axillary nodes to the prognosis of patients with primary breast cancer. An NSABP update. Cancer 1983;52:1551-7.
- 15) Cote RJ, Peterson HF, Chaiwun B, Gelber RD, Goldhirsch A, Castiglione-Gertsch M, et al. Role of immunohistochemical detection of lymph-node metastases in management of breast cancer. International Breast Cancer Study Group. Lancet 1999; 354:896-900.
- 16) Fisher B, Dignam J, Wolmark N, Mamounas E, Costantino J, Poller W, et al. Lumpectomy and radiation therapy for the treatment of intraductal breast cancer: findings from National Surgical Adjuvant Breast and Bowel Project B-17. J Clin Oncol 1998; 16:441-52.
- 17) Frykberg ER, Bland KI. In situ breast carcinoma. Adv Surg 1993;26:29-72.
- 18) Klauber-DeMore N, Tan LK, Liberman L, Kaptain S, Fey J, Borgen P, et al. 2 Sentinel lymph node biopsy: is it indicated in patients with high-risk ductal carcinoma-in-situ and ductal carcinoma-in-situ with microinvasion? Ann Surg Oncol 2000; 7:636-4.
- 19) Pendas S, Dauway E, Giuliano R, Ku N, Cox CE, Reintgen DS. Sentinel node biopsy in ductal carcinoma in situ patients. Ann Surg Oncol 2000;7:15-20.
- 20) Anderson BO. Axillary metastases with DCIS: is the glass half empty or half full? Ann Surg Oncol 2000;7:631-3.
- 21) Linden BD, Zarbo RJ. Cytokeratin immunostaining patterns of benign, reactive lymph node: Applications for the evaluation of sentinel lymph node specimen. Appl Immunohistochem 2001; 9:297-301.