

Estrogen Receptor values in Breast Cancer from Samples for Frozen Section and from Mastectomy Specimens: Preliminary report.

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A prospectivel study was conducted in 20 breast cancer patients who underwent incisional biopsy followed by mastectomy to compare the estrogen receptor (ER) protein values between the biopsy and mastectomy specimens, The average size of the tumor was 6.7 (± 3.5) cm. The mean age of the patients was 46 (± 13) years. There were 12 premenopausal and eight postmenopausal women. The tumor tissue for ER protein assay was from both the biopsy and the mastectomy specimens after the operation had been completed.

ER protein levels averaged 28.2 (± 44) fmol/mg in biopsy specimens and 23.3 (± 49.5) fmol/mg in mastectomy specimens, representing an average fall of 17.4 per cent ($p = 0.179$). Four of 20 tumors (20%) changed from positive ER status in the biopsy specimens to borderline and negative status in the mastectomy specimens. Although the fall in ER values was not statistically significant, we conclude that ER protein assay from biopsy specimens may be more representative of the true ER status than from mastectomy specimens.

Key word : Breast cancer, Estrogen receptor, Biopsy, Mastectomy.

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ผู้ป่วยมะเร็งเต้านม 20 ราย ที่มีก้อนมะเร็งตั้งแต่ขนาด 3 ซม. ขึ้นไป และได้รับการผ่าตัด *incisional biopsy* ตามด้วย *mastectomy* ได้รับการศึกษาแบบไปข้างหน้าเพื่อเปรียบเทียบค่าของ *estrogen receptor (ER)* จากชิ้นเนื้อ *biopsy* และจากชิ้นเนื้อ *mastectomy* ก้อนมะเร็งมีขนาดเฉลี่ย $6.7 (\pm 3.5)$ ซม. ผู้ป่วยมีอายุเฉลี่ย $46 (\pm 13)$ ปี ผู้ป่วย 12 ราย อยู่ในช่วง *premenopause* และ 9 ราย อยู่ในช่วง *post menopause* ระยะเวลาที่ใช้ในการผ่าตัดเฉลี่ย $101 (\pm 45)$ นาที ค่าเฉลี่ยของ *ER* (เมื่อตัดค่าที่เบี่ยงเบนสูงออกไปแล้วหนึ่งราย) ในกลุ่ม *biopsy* เท่ากับ $28.4 (\pm 44)$ *fmol/mg* และในกลุ่ม *mastectomy* เท่ากับ $23.3 (\pm 49.5)$ *fmol/mg* โดยมีค่าแตกต่างลดลง 17.4% แม้จะยังไม่มีความสำคัญทางสถิติ ($P = 0.179$) แต่ก็พบว่าผู้ป่วย 4 ราย จาก 20 ราย (20%) มีผล *ER* เปลี่ยนจากบวกในกลุ่ม *biopsy* เป็นลบและ *borderline* ในกลุ่ม *mastectomy* ผลงานนี้แสดงให้เห็นว่าค่า *ER* จากเนื้อ *biopsy* น่าจะใกล้เคียงกับค่า *ER* ที่แท้จริงของมะเร็งมากกว่าค่า *ER* ที่ได้จากชิ้นเนื้อ *mastectomy*

Estrogen receptor (ER) protein assay has an important role in the management of breast cancer. Patients whose tumors had a high level of ER protein were found to have a greater response to endocrine therapy and a better survival rate than those who had a low level or absent receptor proteins in their tumors.^(1,2) It is therefore essential that ER protein assay should be as accurate as possible to reflect the true receptor status of the tumors, so that response to therapy and prognosis could be predicted with confidence.

Since hormone receptors are very labile proteins, tissue collection is critical in the performance of receptor assay.⁽³⁾ During operation, an incisional biopsy is often performed for confirmation of cancer by frozen section. Tumor tissue for ER protein assay is usually obtained from the mastectomy specimen which has been subjected to devascularization and ischemia for a considerable period of time, with a possible resultant decrease in the receptor value. Heat from electrocoagulation and from the room can also cause proteolysis and falsely lower the receptor protein level.⁽²⁾

The purpose of this prospective study was to compare the ER level from an incisional biopsy specimens with the ER level in tumor tissue from the mastectomy specimens.

Materials and Methods

Patients with breast cancer larger than 3 cm in greatest diameter, admitted in the Department of Surgery, Chulalongkorn Hospital from April 1989 to May 1990 were studied.

At the start of operation an incisional biopsy without cauterization was performed. Each specimen was divided into two pieces, one was sent for frozen section biopsy and the other was kept in the freezer. After frozen section confirmation of cancer a mastectomy was undertaken. At the completion of mastectomy a second specimen was taken from the

biopsy site and frozen. Both frozen specimens were labelled and sent to the Cancer Institute in an icebox for ER protein assay.

At the Cancer Institute, both specimens were kept at -70°C and the ER proteins were assayed using the polyethyleneglycol method of Braunsberg. The unbounded receptor sites were measured. A receptor value of less than 3 fmol/mg protein was considered negative, between 3 and 10 fmol/mg borderline, from 10 fmol/mg to 100 positive, and above 100 fmol/mg strongly positive.⁽²⁾

Results

Twenty breast cancer patients were studied, the average age was 46 (± 13) years, range 30 to 73 years. Twelve patients were premenopausal and eight were postmenopausal. The average size of the tumor was 6.7 (± 3.5) and the operating time was 101 (± 45) minutes. The histologic types were infiltrating ductal carcinoma in 18 cases, medullary in one and papillary in one. The overall data for the 20 patients are shown in table 1.

In the biopsy specimens, 60% (12 of 20) of the tumors were found to be ER positive and 40% (8/20) were ER negative. In the mastectomy specimens, only 40% (8/20) were ER positive, 10% (2/20) were borderline, and 50% (10/20) were ER negative (table 2).

When data of the ninth patient with abnormally high ER values were excluded, the mean ER value for the biopsy specimens was 28.2 (± 44) fmol/mg and 23.3 (± 49.5) fmol/mg for the mastectomy specimens. This represents a decrease of 17.4% ($P = 0.179$).

Table 3 shows the change in ER status according to Teicher.⁽²⁾ Four of 12 ER positive biopsy specimens changed to ER negative⁽²⁾ and borderline status⁽²⁾ when tissues from the mastectomy specimen were assayed. This represents a change in ER status from estrogen receptor positive to negative or borderline in 20% (4/20) of the patients in the study.

Table 1. Patient data and estrogen receptor protein values.

Patient	Age (year)	Menstrual status	Tumor size (cm.)	Op time (min)	Estrogen receptor protein	
					Biopsy specimen	Mastectomy specimen
1	43	pre	5	50	0	0
2	31	pre	3	51	0	0
3	32	pre	4	105	23.3	36
4	39	pre	6	45	155.6	210.7
5	38	pre	6	150	0	0
6	30	pre	10	50	29.2	27.8
7*	39	pre	4	170	0	0
8	37	pre	3	150	0	0
9	69	post	7	75	1709	1627.7
10	41	pre	8	50	137.3	75.7
11	73	post	7	40	24.2	0
12	36	pre	4	120	22.8	35.7
13**	45	pre	17	105	25.1	7.0
14	40	pre	5	105	11.1	7.9
15	49	pre	10	110	0	0
16	62	post	8	160	49.6	22.4
17	58	post	4	150	0	0
18	62	post	4	160	27.8	0
19	40	pre	12	105	0	0
20	57	post	6	70	29.9	19.9

*Medullary carcinoma

**Papillary carcinoma

Table 2. Estrogen receptor status.

ER Status	Biopsy specimen N = 20	Mastectomy specimen N = 20
Positive	12(60%)	8(40%)
Borderline	—	2(10%)
Negative	8(40%)	10(50%)

Table 3. Change in ER status*.

Biopsy	Mastectomy
3 Strongly positive	2 Strongly Positive
	1 Positive
9 Positive	5 Positive
	2 Borderline
	2 Negative
8 Negative	8 Negative

*According to Teicher.⁽²⁾

Discussion

It is generally recognized that surgery alone may be inadequate therapy for the majority of breast cancer patients who may already have micrometastasis at the time of diagnosis. Consequently multimodality treatment comprising surgery, radiotherapy and systemic therapy is becoming increasingly popular. Systemic therapy consists of either chemotherapy or hormonal therapy. The accurate selection of patients for hormonal therapy is important for optimum results. ER status has been shown to be a good predictor of response to hormonal therapy.

The ER value depends on many factors such as the patient's menopausal status, tumor histology^(1,5) and methods of specimen collection. ER is a heat labile protein, and can be denatured easily even at room temperature.^(1,3) Most reports suggested that specimens should be transported in dry ice and kept in liquid nitrogen for not more than 4 weeks before analysis.⁽³⁾ Some reports suggested that the samples from biopsy specimens rather than the mastectomy specimens should be used for analysis.^(2,4,16)

This study used patients as their own controls, thus reducing several confounding variables which could have affected the ER values. The sample size is however too small to show any statistical significance. In three patients the ER values from mastectomy specimens were higher than from biopsy specimens, one reason could be the inhomogenous distribution of ER receptors in the tumors.⁽⁷⁾ Although fine needle aspiration cytology has become an important diagnostic tool in cancer, the tissue obtained is inadequate for hormone assay by the standard methods.⁽⁶⁾ Therefore tumor tissues from mastectomy specimens, are still frequently used for ER assay. Our results suggested that the ER status from biopsy specimens may be more representative of the true ER status of the tumors than tissue from mastectomy specimens.

Conclusion

A prospective study was conducted to compare

tumor ER values from biopsy and mastectomy specimens in 20 breast cancer patients. The ER values were found to be higher in the biopsy than in the mastectomy specimens, although the difference was not statistically significant. We conclude that ER protein assay from biopsy specimens may be more representative of the true ER status than from mastectomy specimens.

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