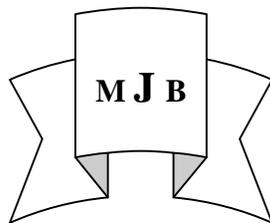# A Retrospective Study of Relapsed Breast Cancer Cases During Follow-Up in Merjan

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Abstract

Breast cancer patients are routinely followed after primary treatment. Many intensive diagnostic methods (tumor markers, chest x-ray, mammogmphy, liver sonar, bone scans) are performed periodically.
However, it remains to be determined how often attempts should be made to detect the first recurrence of breast cancer by these methods.

To evaluate the effect of imaging diagnosis and tumor markers, we analyzed methods of detection of first recurrence sites during intensive follow-up of breast cancer patients. Of 550 female patients who had been surgically treated between march 2004 and December 2007, 65 recurrent cases had been diagnosed as of July 2008.

Thirty cases (46%) had been found as a result of symptoms related to the site of recurrence and 14 cases (22%) were detected by physical examination.

In the remaining 21 cases (32%), detection was by other methods: in eight cases by imaging diagnosis, in three cases based on abnormal tumor markers and in 10 cases by imaging diagnosis and abnormal tumor markers.
There was a significant difference between first recurrence sites (loco-regional, bone and viscera) and the methods of detection (symptoms, physical examination and other diagnostic methods) ($p<0.0001$).

However, no statistical difference in overall survival after operation was observed between the 30 cases found as a result of symptoms and the 35 cases detected by physical examination or other diagnostic methods, Period of fellow up extend between 6-45 months post operative .

دراسة لحالات الانتكاسة المرضية للمصابين بسرطان الثدي اثناء فترة المتابعة

الخلاصة

من اجل تقييم تاثير الطرق التشخيصية للمرضى المصابين بسرطان الثدي، تم اخذ عينة تشمل 550 مريضة مصابة بسرطان الثدي والمجراة لهن عمليات جراحية للفترة من اذار 2004 لغاية ك1 2007. تم تشخيص 65 حالة انتكاسة بحلول تموز 2008 . 30 حالة (46%) تـم تشخيصهم اعتمادا على الاعراض المصاحبة للعضو المصاب. 14 حالة (22%) تم تشخيصهم عن طريق الفحص السريري21 حالة (32%) تم تشخيصهم بطرق اخرى وتشمل:8حالات عن طريق اجراء الفحوص الشعاعية3 حالات عن طريق فحص الدم (معلمـات الاورام) 10 حالات بواسطة الاثنين معا يوجد فرق واضح بين موضع الانتكاسة والطريقة التي يتم بها تشخيص المرض، علما بانه لايوجد فرق في معدل البقاء بعد العملية بين الثلاثين مريضا(المشخصة لديهم حالات الانتكاسة اعتمادا على الاعراض المرضية) عن الخمسة والثلاثـين مريـضا المشخصين بالطرق الاخرى ، علما بان فترة المتابعة انحصرت بين 6 – 45 شهر بعد العملية .

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Introduction

Surgical, medical and radiological treatments can prolong the disease-free survival of operable breast cancer patients once breast cancer has recurred, it is generally considered incurable. [1]

Breast cancer surveillance is necessary to detect early recurrence, one reason is that the sooner any recurrence is detected, the more

effectively medical or other treatment may be administered[1].

However, there has been no clear evidence whether intensive follow-up of breast cancer patients results in survival benefit. The optimum cost-benefit relation ship of follow-up of breast cancer also remains to be determined [2,3].

The surveillance guidelines recommended by American society of clinical oncology (ASCO) in 1997 [4] caused us to reflect on the usual follow-up methods. Asco's expert panel recommended monthly breast self-examination, annual mammography, a careful history and physical examination every 3-6 months for 3 years, then every 6-12 months for the following 2 years.

The value of intensive diagnostic methods (tumor markers, chest X ray, liver sonar and bone scan) could not be confirmed.

To evaluate the effect of imaging diagnosis and tumor markers, we retrospectively analyzed methods of detection of first recurrence sites during intensive follow-up of breast cancer patients.

Patients and Methods

Total mastectomy or conservative mastectomy with axillary dissection was performed in 550 cases of female breast cancer between March 2004 and December 2007.

Adjuvant chemotherapy and/or Hormonal therapy were preformed in 358 of the 550 cases (65%) and adjuvant radiation therapy in 61 cases (11%) regardless of whether adjuvant therapy was preformed or not, most patients were scheduled to be followed up at routine appointments every 1-4 months for 2 years after operation and then every 4-6 months for the following 3 years. Patients complaints were recorded: pain, fatigue, nausea, dyspnea, cough, hoarseness, dizziness, abdominal discomfort and also whether they had noticed amass in the chest, breast, axillary or cervical regions. Periodic examinations consisted of a full history, physical examination, complete blood cell count and blood chemistry studies, including tumor markers (CEA,CA15-3) every 1-4 months, chest X-ray every 6 months, mammogram every 6-24 months and liver sonar every 3 months. No gynecological examination was usually performed if any signs or symptoms of recurrence developed, more intensive imaging diagnosis, including computed tomography and magnetic resonance imaging, was carried out.

In addition, loco regional recurrent lesions were confirmed by aspiration biopsy cytology or exisional biopsy. Stastical significanse was determined by using the chi-squared test.

Results

As of July 2008, 65 cases had been diagnosed as having first recurrence in this division. The characteristics of the recurrent cases are shown in table 1.

About one third of recurrent cases were in more advanced clinical stages and had 10 or more nodal metastases. Most patients had received adjuvant chemo therapy and\or hormonal therapy. The first sites detected in the table means lesions diagnosed as recurrence on the basis of symptoms or after routine surveillance without symptoms. The 16 cases of local lesions consisted of 13 cases of chest

wall recurrence, one case of axillary lymph node and two cases of conserved breast recurrence.

Table 2 shows the correlation between first recurrence sites and methods of detection. Thirty cases (46%) had been found as a result of symptoms at the recurrence sites and 14 case (22%) had been detected by physical examination.

In the remaining 21 cases(32%) detection was by other methods. In eight cases by imaging diagnosis, in three cases based on abnormal tumor markers and in 10 cases by imaging diagnosis and abnormal tumor markers. There was a significant difference between first recurrence sites (loco-regional, bone and viscera) and methods of detection (symptoms, physical examination and other methods) (p<0.0001). imaging diagnosis and tumor markers were more effective in detecting lung, liver and bone metastases than physical examination. however, 14 cases

(22%) of distant metastases were diagnosed as a result of symptoms related to the site of recurrence.

We compared the clinicopathological features and survival curve of the 30 cases with symptoms and the 35 cases without symptoms detected by physical examination, imaging diagnosis or tumor markers (table 3).

There were no significant difference in age, clinical stage, nodal metastases, adjuvant therapy, disease free interval or final recurrence sites after systemic surveillance between the two groups. There was no stastical difference between them in overall survival after operation.

There was a significant difference between first recurrence sites(loco-regional, bone, and viscera) and the methods of detection (symptoms, physical examination and imaging diagnosis, including tumor markers) by using the chi-squared test (p<0.0001).

Table 1 Patient characteristics and first recurrence sites

Characteristics	No. of cases	%
Recurrent cases	65	100
Age/years		
<35	5	8%
30-50	32	49%
51+	28	43%
Menopausal status		
Pre menopause	37	57%
Post menopause	28	43%
Stage		
I	8	12%
IIA,IIB	37	57%
IIIA,IIIB	20	31%
Histological sub type		
Invasive ductal carcinoma	60	92%
Invasive lobular carcinoma	2	3%
Others	3	5%
Nodal metastases		
0	15	23%
1-9	29	45%
10	21	32%
Surgical procedure		
Total mastectomy	59	91%
Partial mastectomy	6	9%
Adjuvant therapy		
No therapy	6	9%
Hormonal therapy	5	8%
Chemo therapy	23	35%
Chemo hormonal therapy	31	48%
Radiation therapy	2	3%
Disease- free interval (days)		
>365	24	37%
366-730	20	31%
731+	21	32%
First sites detected		
-local lesion (skin, ipsilateral axilla and breast)	16	25%
-regional lymph node	12	18%
-loco-regional lesions	1	2%
-bone	14	22%
-lung	8	12%
-liver	5	8%
-brain	2	3%
-multiple organs	7	11%

Table 2 Methods of detection of first recurrence sites (No. of cases)

Method	Loco regional	Bone	Lung	Liver	Brain	multiple
● Symptoms (30)	16	6	1	1	2	4
● Physical examination (14)	13	1	0	0	0	0
● Imaging diagnosis (8)	0	2	6	0	0	0
● Tumor markers (3)	0	1	0	1	0	1
● Imaging diagnosis and tumor markers (10)	0	4	1	3	0	2
● Total (65)	29	14	8	5	2	7

Table 3 Comparison of clinicopathological features of cases with and without symptoms at the time of detection of the first recurrence.

Characteristics	No. of recurrence cases		P value
	Symptoms	**No symptoms**	
Age(years) <35 36-50 51+	2 15 13	3 17 15	0.959
Stage I IIA,IIB IIIA,IIIB	5 16 9	3 21 11	0.607
Nodal metastases 0 1-9 10	6 14 10	9 15 11	0.869
Adjuvant therapy No therapy Hormonal therapy Chemo hormonal therapy	4 3 23	2 2 31	0.432
Disease free intervals (days) <365 365-730 731+	13 9 8	11 11 13	0.554
Final recurrence Sites after Systemic surveillance Loco regional Bone or lung* Liver or brain Multiple organs *	12 9 3 6	12 16 4 3	0.434

* including some cases with loco- regional recurrence

Discussion

In most cases, physical and diagnostic examinations were performed at routine appointments. Nevertheless, 46% of the patients with recurrences presented with symptoms and 54% of them had been detected by physical examination, imaging diagnosis or

abnormal tumor markers. Several other investigators have also reported negative results of systemic surveillance of breast cancer patients [5-8],Symptomatic first recurrence ranged between 77 and 91% in their reports.

In contrast, asymptomatic first recurrence detected by physical examination or other diagnostic methods ranged between 9 and 46%.

Distant organ metastases may be more frequently found by chest X-ray, bone scans and other imaging diagnosis [9]. Tumor markers may be helpful in evaluating the extent of metastatic breast cancer [10].

However, survival benefit derived from intensive follow-up has not been confirmed. In the present cases, overall survivals in the symptomatic and asymptomatic recurrence groups were similar. One explanation may be that many cases had early recurrence within 2 years and early recurrence resulted in more rapid progression.

In a randomized trial in Italy, the 5-year overall survival in the intensive follow-up group could not be prolonged compared with the control follow-up group [9]. routine examinations including chest X-ray, bone scans, liver sonar, annual mammography and tumor markers failed to result in improvements in the out come of patients with recurrent breast cancer.

Most patients are usually informed of prognostic factors in resected specimens, such as histological grade, number of nodal metastases and hormonal receptor status. They are also informed about the risk of breast cancer recurrence and whether they need to undergo adjuvant therapy.

Many patients, especially those with high risk breast cancer, may prefer more intensive follow-up for their emotional well-being and for high quality of life. However, a randomized trial demonstrated that the intensive follow-up did not affect health related quality of life in breast cancer patients i.e.overall health and quality of life perception, emotional well-being, body image, satisfaction with care etc [11].

Conclusions

Taken together with ASCO's surveillance guide lines, systemic surveillance of breast cancer is not always necessary for all breast cancer patients.

A careful history and physical examinations are in practice recommended every 3-6 months for 3 years and then every 6 months for the following 2 years.

At least, intensive follow-up should be limited to high-risk breast cancer patients with positive nodes, high histological grade and especially those who enter randomized clinical trials.

Recommendation

This study needs more time for follow up of patients because this period of follow up is too short to assess the survival rate .

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