# Exploring Breast Cancer Data to Find the Risk Factors for Distant Metastasis: Register Data, The National Cancer Institute of Thailand

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## ABSTRACT

A retrospective cohort of registered breast cancer patients at the National Cancer Institute of Thailand in 2004 was investigated to explore the association of prognostic factors with the probability of distant metastasis. The analysis was done using binary and ordinal logistic regression models. There were 893 breast cancer patients included in a 3 year follow up study. During the study period 129(14.45%) were reported as metastasis cases, which the highest number of metastasis patients was found in bone (47.3%). The prognostic variables related to the distant metastasis breast cancer using binary logistic regression model were found among vascular invasion (OR = 8.8), histologic grade III (OR = 2.9), lymphatic invasion (OR = 2.4), estrogen receptor (OR = 2.2), progesterone receptor (OR = 2.0), p53 (OR = 1.8), tumor size (OR = 1.2), radiation therapy (OR = 0.5) and hormonal therapy (OR = 0.4). Patients in which metastasis occurred within the 1st, 2nd and 3rd years after initial diagnosis were 75, 28 and 26 cases respectively. Using an ordinal logistic regression model, the prognostic factors included vascular invasion (OR = 5.6), estrogen receptor (OR = 2.3), lymphatic invasion (OR = 2.3), histologic grade III (OR = 1.9), p53 (OR = 2.0), tumor size (OR = 1.2), radiation therapy (OR = 0.6) and hormonal therapy (OR = 0.5). The prognostic factor of vascular invasion showed the highest OR in this study. Another group of variables with moderate OR were estrogen receptor, lymphatic invasion, histologic grade III, p53 and tumor size. The adjuvant therapies were protective factors (OR < 1). A follow up system for those at risk for metastasis is suggested.

***Key words:*** breast cancer, distant metastasis breast cancer, prognostic factors

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## Introduction

Breast cancer continues to be the most commonly diagnosed cancer in women in the developed world[1]. Breast cancer prognosis factors include, for example, morphological, pathological tumor specification and biological tumor markers. A distant breast cancer recurrence, also called a metastasis is the most dangerous type of recurrence[2]. The major cause of death from breast cancer is the metastatic spread from the primary tumor to distant sites of the body[3]. Approximately 10-15% of aggressive breast cancer disease develop distant metastasis within 3 years after the initial detection of the primary tumor[4]. If the primary and adjunctive therapies are not totally effective to the eradication of all diseases, breast cancer can metastasis to other parts of the body.

Although the curative management for breast cancer has been improved continuously, low sensitivity to chemotherapeutic drugs after long time use and distant metastasis are still the main factors related to a patient's survival without distant metastasis[5]. Furthermore, pathological signs such as abnormal levels of biomarkers are challenged in metastatic breast cancer.

The objectives of this study were to examine the effect of prognostic predictors of general patient characteristics, clinical-pathological characteristics, type of surgery and adjuvant therapy on patient clinical outcome of distant metastasis. Binary logistic regression and ordinal logistic regression models were applied to breast cancer patients registered in the National Cancer Institute (NCI) of Thailand whose initial diagnosis and treatment was from January- December 2004.

## Methods

The NCI is the national organization solely dedicated to cancer research and activities such as conducting and fostering cancer research, reviewing and approving grant in aid applications to support promising research projects on the cause, prevention, diagnosis and treatment of cancer. The research project was approved by two ethical committees: The Faculty of Public Health Mahidol University MUPH 2008-038 and The National Cancer Institute of Thailand document paper no 039/2551.

## Patients

A retrospective cohort study consisted of 980 female breast cancer patients registered and diagnosed at the NCI during January-December 2004; the follow up period for each patient was 3 years, thus ended during January-December 2007. Inclusion criteria were set as patients who registered at the NCI with initially diagnosed and primarily treated breast cancer; the exclusion criteria covered breast cancer patients with tumors at other organs and distant metastasis as initially diagnosed, or incomplete follow up during the study period.

### Statistical analysis

The prognostic factors included demographic characteristics (age of patient at initial breast cancer diagnosis), tumor characteristic and clinico-pathological characteristics based on pathology reports and laboratory reports, type of surgery and adjuvant treatments. The outcome variable was distant metastasis conditions within 3 years after initial diagnosis.

Univariate analysis used for testing association and/or differences between groups were chi-square test, or Fisher's Exact test or Student's t-test. Binary logistic regression was used to investigate the relationship between predictor variables and the probability of distant metastasis breast cancer. The model was generated to predict a logit transformation of the probability

of presence of distant metastasis in breast cancer patients. Ordinal logistic regression was used to investigate the relationship between predictor variables and the probability of distant metastasis that occur in the first, second and third years after diagnosis. The outcome variable was classified into 4 condition levels of breast cancer patients. The non distant metastasis patients implied least aggressive condition (level 1). The distant metastasis in the 3rd year after diagnosis (26 patients) implied mild aggressive condition (level 2). The distant metastasis in the 2nd year after diagnosis (28 patients) implied moderate aggressive condition (level 3). The distant metastasis in the 1st year after diagnosis (75 patients) implied severe aggressive condition (level 4).

## Results

### Characteristics of the patients

In 2004, 980 women patients were diagnosed with breast cancer. Eighty seven patients were excluded from the study including 60 patients who had distant metastatic disease at the time of first diagnosis and 27 patients lost from physician's follow up or died from other reasons without distant metastasis. The total of 893 eligible patients were followed up until 2007. At the end of the follow up period there were 129 (14.45%) breast cancer patients with distant metastasis; the average age was 49.68 ± 10.95 years (min-max=21-87), the a highest frequency of 330 (37%) was in 40-49 years. The lower age groups appeared to have higher percentage of metastasis. The tumor sizes ranged from 0.1 to 13.3 cm. (median tumor size 2.5 cm.). The tumor size of < 2 cm., 2-5 cm. and > 5 cm. were found in 186(20.8%) patients, 606(67.9%) and 101 (11.3%) patients, respectively.

The 583(65.3%) patients had tumors located in the lateral breast, 154(17.2%) in medial part of tumor, 68(7.6%) in central nipple area and 88(9.9%) in overlapping of breast. Of those 91(15.6%) of the distant metastasis breast cancer patients were in lateral breast and 29(3.3%) patients had multiple tumors.

### Clinico-pathological characteristics of tumor classified by non-distant metastasis and distant metastasis breast cancer

Half of the patients were in histologic grade II and about 10% got metastasis, whereas 25% got metastasis while they were in histologic grade III. The patients ranged in number of lymph node invasion from 0 to 23 nodes: half of the patients had none. The 89(10%) patients got lymph node invasion in more than 10 nodes, and 34 patients got distant metastasis. Vascular invasion was detected in 69(7.7%) patients, and 42 patients got distant metastasis. Lymphatic invasion was detected in 155(17.4%) patients, and 54 patients got distant metastasis.

It should be noted that 461(51.6%) patients were estrogen receptor positive whereas 282(31.6%) patients were progesterone receptor positive. HER-2/neu protein was over-expressed in 285(31.9%) patients, while p53 gene was mutation in 338(37.8%) patients.

### Surgery and adjuvant therapy of tumor classified by non distant metastasis and distant metastasis breast cancer

The 17(1.9%) patients were treated with breast conservation (lumpectomy). Considering adjuvant therapy, 434 (48.6%) patients received adjuvant radiation therapy, 819(91.7%) patients received adjuvant chemotherapy and 361(40.4%) patients received adjuvant hormone therapy. Details of general and pathological characteristics, type of surgery and adjuvant therapy of breast cancer patients are shown in table 1.

**Table 1** General and pathological characteristics, type of surgery and adjuvant therapy of patients at initial diagnosis classified by non-distant metastasis and distant metastasis

| Characteristics | Number (%) | | Non-distant metastasis (%) | | Distant - metastasis (%) | |
|---|---|---|---|---|---|---|
| total | 893 | | 764 | | 129 | |
| **Age** | median 49 (range 21-87) | | | | | |
| < 40 years | 140 | (15.7) | 119 | (85.0) | 21 | (15.0) |
| 40 - 49 years | 330 | (37.0) | 280 | (84.8) | 50 | (15.2) |
| 50 - 59 years | 267 | (29.9) | 228 | (85.4) | 39 | (14.6) |
| 60 - 69 years | 103 | (11.5) | 91 | (88.3) | 12 | (11.7) |
| 70 + years | 53 | (5.9) | 46 | (86.8) | 7 | (13.2) |
| **Tumor location** | | | | | | |
| Medial | 154 | (17.2) | 138 | (89.6) | 16 | (10.4) |
| Lateral | 583 | (65.3) | 492 | (84.4) | 91 | (15.6) |
| Nipple area | 68 | (7.6) | 59 | (86.8) | 9 | (13.2) |
| Overlapping | 88 | (9.9) | 75 | (85.2) | 13 | (14.8) |
| **Tumor size** | median 2.5 (range 0.1-13.3) | | | | | |
| < 2 cm. | 186 | (20.8) | 170 | (91.4) | 16 | (8.6) |
| 2 - 5 cm. | 606 | (67.9) | 537 | (88.6) | 69 | (11.4) |
| > 5 cm. | 101 | (11.3) | 57 | (56.4) | 44 | (43.6 |
| **Multiple tumor** | | | | | | |
| Absence | 864 | (96.8) | 741 | (85.8) | 123 | (14.2) |
| Presence (Multifocal) | 14 | (1.6) | 13 | (92.9) | 1 | (7.1) |
| Presence (Multicentric) | 15 | (1.7) | 10 | (66.7) | 5 | (33.3) |
| **Histologic Grade** | | | | | | |
| Grade I | 111 | (12.4) | 106 | (95.5) | 5 | (4.5) |
| Grade II | 459 | (51.4) | 417 | (90.8) | 42 | (9.2) |
| Grade III | 323 | (36.2) | 241 | (74.6) | 82 | (25.4) |
| **Lymph node invasion** | | | | | | |
| None | 459 | (51.4) | 420 | (91.5) | 39 | (8.5) |
| 1 - 3 nodes | 196 | (21.9) | 172 | (87.8) | 24 | (12.2) |
| 4 - 10 nodes | 149 | (16.7) | 117 | (78.5) | 32 | (21.5) |
| > 10 nodes | 89 | (10.0) | 55 | (61.8) | 34 | (38.2) |
| **Vascular invasion** | | | | | | |
| Negative | 824 | (92.3) | 737 | (89.4) | 87 | (10.6) |
| Positive | 69 | (7.7) | 27 | (39.1) | 42 | (60.9) |
| **Lymphatic invasion** | | | | | | |
| Negative | 738 | (82.6) | 663 | (89.8) | 75 | (10.2) |
| Positive | 155 | (17.4) | 101 | (65.2) | 54 | (34.8) |
| **Estrogen receptor** | | | | | | |
| Negative | 432 | (48.4) | 427 | (92.6) | 34 | (7.4) |
| Positive | 461 | (51.6) | 337 | (78.0) | 95 | (22.0) |
| **Progesterone receptor** | | | | | | |
| Negative | 611 | (68.4) | 262 | (92.9) | 20 | (7.1) |
| Positive | 282 | (31.6) | 502 | (82.2) | 109 | (17.8) |

**Table 1** General and pathological characteristics, type of surgery and adjuvant therapy of patients at initial diagnosis classified by non-distant metastasis and distant metastasis (cont.)

| Characteristics | Number (%) | | Non-distant metastasis (%) | | Distant - metastasis (%) | |
|---|---|---|---|---|---|---|
| **p53** | | | | | | |
| Negative | 555 | (62.2) | 500 | (90.1) | 55 | (9.9) |
| Positive | 338 | (37.8) | 264 | (78.1) | 74 | (21.9) |
| **HER-2 over-expression** | | | | | | |
| Negative | 608 | (68.1) | 541 | (89.0) | 67 | (11.0) |
| Positive | 285 | (31.9) | 223 | (78.2) | 62 | (21.8) |
| **Type of surgery** | | | | | | |
| Mastectomy | 876 | (98.1) | 749 | (85.5) | 127 | (14.5) |
| Lumpectomy | 17 | (1.9) | 15 | (88.2) | 2 | (11.8) |
| **Radiation therapy** | | | | | | |
| Received | 434 | (48.6) | 347 | (80.0) | 87 | (20.0) |
| Not received | 459 | (51.4) | 417 | (90.9) | 42 | (9.1) |
| **Chemotherapy** | | | | | | |
| Received | 819 | (91.7) | 698 | (85.2) | 121 | (14.8) |
| Not received | 74 | (8.3) | 66 | (89.2) | 8 | (10.8) |
| **Hormonal therapy** | | | | | | |
| Received | 361 | (40.4) | 305 | (84.5) | 56 | (15.5) |
| Not received | 532 | (59.6) | 459 | (86.3) | 73 | (13.7) |

**Metastasis according to sites in the three consecutive years after initial diagnosis**

The 75(58.14%), 28(21.70%) and 26 (20.16%) patients had distant metastasis in first, second and third years after initial diagnosis, respectively. Most of distant metastasis breast cancer in all sites was reported in the first year after initial diagnosis. Bone was the most frequent metastatic site in every year after initial diagnosis. Detail of distant metastasis is shown in table 2.

**Table 2** The number of breast cancer according to sites of distant metastasis in three years after initial diagnosis

| Sites of distant metastasis | Years of distant metastasis | | | Total |
|---|---|---|---|---|
| | 1st year | 2nd year | 3rd year | |
| **bone** | 32 | 15 | 14 | 61 |
| **lung** | 17 | 4 | 4 | 25 |
| **liver** | 8 | 4 | 4 | 16 |
| **brain** | 2 | 1 | 0 | 3 |
| **bone and lung** | 4 | 1 | 1 | 6 |
| **bone and liver** | 5 | 3 | 2 | 10 |
| **bone and brain** | 1 | 0 | 0 | 1 |
| **lung and liver** | 3 | 0 | 0 | 3 |
| **liver and brain** | 1 | 0 | 0 | 1 |
| **bone, lung and liver** | 1 | 0 | 0 | 1 |
| **bone, liver and brain** | 1 | 0 | 0 | 1 |
| **bone, lung, liver and brain** | 0 | 0 | 1 | 1 |
| **Total** | **75** | **28** | **26** | **129** |
| | **58.14%** | **21.70%** | **20.16%** | **100%** |

**Relationship between predictor variables and distant metastasis breast cancer**

According to univariate analysis, 9 variables which were found to be significantly associated with distant metastasis breast cancer were tumor size, histologic grade, vascular invasion, lymphatic invasion, estrogen receptor, progesterone receptor, p53, adjuvant radiation therapy and adjuvant hormonal therapy. The binary logistic regression model with entering of all significant predictor variables in one step, was set along with summarizing statistics, coefficient, estimated odds ratios and 95% confidence interval as shown in table 3.

**Table 3** Summarized the statistics, coefficient, estimated odds ratio and 95% confidence interval by binary logistic regression analysis

| Variables | β | Wald Test | *p-value* | Odds Ratio | 95% Confidence Interval for Odds Ratio | |
|---|---|---|---|---|---|---|
| | | | | | Lower | Upper |
| **tumor size** | 0.192 | 9.090 | 0.003 | 1.212 | 1.070 | 1.373 |
| **histologic grade III** | 1.068 | 4.345 | 0.037 | 2.908 | 1.066 | 7.935 |
| **vascular invasion** | 2.173 | 44.132 | 0.000 | 8.785 | 4.627 | 16.679 |
| **lymphatic invasion** | 0.879 | 10.511 | 0.001 | 2.409 | 1.416 | 4.098 |
| **ER negative** | 0.797 | 7.856 | 0.005 | 2.218 | 1.271 | 3.872 |
| **PR negative** | 0.713 | 4.678 | 0.031 | 2.039 | 1.069 | 3.890 |
| **p53** | 0.595 | 6.399 | 0.011 | 1.812 | 1.143 | 2.873 |
| **without radiation therapy** | - 0.635 | 6.965 | 0.008 | 0.530 | 0.331 | 0.849 |
| **without hormonal therapy** | - 0.857 | 10.833 | 0.001 | 0.425 | 0.255 | 0.707 |
| **constant** | - 4.122 | 50.389 | <0.0001 | | | |

$R^2$ = 38.5%

According to table 3, vascular invasion was found to be the strongest risk factor for distant metastasis of breast cancer (OR = 8.79, 95% CI = 4.63-16.68). The moderate level of odds ratio were histologic grade III (OR = 2.91, 95% CI = 1.07-7.94), lymphatic invasion (OR = 2.41, 95% CI = 1.42-4.10), estrogen receptor (OR = 2.22, 95% CI = 1.22-3.87) and progesterone receptor (OR = 2.04, 95% CI = 1.07-3.89). At the lower level of OR were p53 (OR = 1.81, 95% CI = 1.14-2.87) and tumor size (OR = 1.21, 95% CI = 1.07-1.37). The last group of predictor variables had negative coefficient were adjuvant radiation therapy (OR = 0.53, 95% CI = 0.33- 0.85) and hormonal therapy (OR = 0.43, 95% CI = 0.26-0.71). The $R^2$ in this model equaled 38.5%. This binary logistic model explained 38.5% of variability in predicted variables toward the probability of distant metastasis breast cancer.

**Non-distant metastasis and distant metastasis in each consecutive year of treatment**

order 1 → non - distant metastasis (least aggressive)

order 2 → metastasis in 3rd year of treatment (mild aggressive)

order 3 → metastasis in 2nd year of treatment (moderate aggressive)

order 4 → metastasis in 1st year of treatment (severe aggressive)

**Table 4** Summarized the statistics, intercepts, coefficients(β), estimated odds ratio and 95% confidence interval from ordinal logistic regression

| Variables | Coefficient | Wald Test | *p-value* | Odds Ratio | 95% Confidence Interval for Odds Ratio | |
|---|---|---|---|---|---|---|
| | | | | | Lower | Upper |
| **Intercept 1**($\hat{\alpha}_1$) | -4.970 | | | | | |
| **Intercept 2**($\hat{\alpha}_2$) | -5.338 | | | | | |
| **Intercept 3**($\hat{\alpha}_3$) | -5.825 | | | | | |
| | **coefficient**(β) | | | | | |
| **tumor size** | 0.215 | 15.742 | <0.0001 | 1.240 | 1.115 | 1.380 |
| **histologic grade III** | 0.659 | 10.870 | 0.001 | 1.933 | 1.306 | 2.861 |
| **vascular invasion** | 1.725 | 32.924 | <0.0001 | 5.612 | 3.081 | 10.223 |
| **lymphatic invasion** | 0.825 | 10.302 | 0.001 | 2.282 | 1.379 | 3.776 |
| **ER negative** | 0.827 | 8.834 | 0.003 | 2.286 | 1.326 | 3.943 |
| **p53** | 0.681 | 9.027 | 0.003 | 1.976 | 1.266 | 3.083 |
| **without radiation therapy** | -0.594 | 6.318 | 0.012 | 0.552 | 0.348 | 2.404 |
| **without hormonal therapy** | -0.762 | 9.402 | 0.002 | 0.467 | 0.287 | 0.760 |

$R^2$ = 33.3%

According to the ordinal logistic regression, vascular invasion was the strongest risk of distant metastasis breast cancer (OR = 5.61, 95% CI = 3.08-10.22). Moderate risk of distant metastasis breast cancer were lymphatic invasion (OR = 2.28, 95% CI = 1.38-3.78) and estrogen receptor (OR = 2.29, 95% CI = 1.33-3.94). Lower risk of distant metastasis were tumor size (OR = 1.24, 95% CI = 1.12-1.38), histologic grade III (OR = 1.93, 95% CI = 1.31-2.86) and p53 (OR = 1.98, 95% CI = 1.27-3.08). Last group for odds ratio less than 1 were radiation therapy (OR = 0.55, 95% CI = 0.35-0.88) and hormonal therapy (OR = 0.47, 95% CI = 0.29-0.76). The $R^2$ in this model equaled 33.3%. This ordinal logistic model explained 33.3% of variability in predicted variables toward the probability of distant metastasis breast cancer.

## Discussion

Logistic regression analysis provides a proper model of statistical prognosis for certain types of endpoints in patients[6,7]. In this study, binary logistic regression was employed to assess factors associated with metastasis in breast cancer patients. In addition, the occurrance of distant metastasis in ordinal years of treatment i.e. first year, second year and third year could be considered as severity levels of the cases: the ordinal logistic regression analysis, known as the

proportional odds model, was thus employed to determine the model at each consecutive year after treatment. The odds ratio is assumed to be constant for all ordinal logistic models. This property can be tested from the coefficients(β) by parallel test with chi-square test. The coefficients for the variables in the equations would not vary significantly if coefficients were estimated separately or slopes would be the same. The same test as parallel test is chi- square score test for the proportional odds assumption. A non-signifi cant test is taken as evidence the coefficients(β) are parallel and that the odds ratio can be interpreted as constant across all possible cutpoint of the outcome[8].

The 14.45% or 129 out of 893 breast cancer patients, descriptively got metastasis within 3 years of followed up. Approximately 10-15% of patients with breast cancer have an aggressive disease and developed distant metastasis within 3 years after the initial detection of the primary tumor[4].

Consideration of age at diagnosis, patients under 50 years of age had distant metastasis breast cancer for approximately 15%, whereas less than 15% was found in patients with age at diagnosis over 50 years. At The University of Texas M.D. Anderson Cancer Center from 1982 to 2002, among 226 breast cancer patients who had a pathologic complete response after neoadjuvant chemotherapy, those aged at diagnosis under 50 years 18.4% was found with distant metastasis and those aged at diagnosis over 50 years 5.9% reported distant metastasis breast cancer[9].

For a group of clinico-pathological characteristics, histologic grade III had the highest frequency of distant metastasis (25.4%). This reflects the fact that a higher grade means higher risk: that is, tumor with more abnormal looking cells tend to grow and spread more quickly[10]. Lymph node involvement between 4-10 nodes and more than 10 nodes had a high percentage of distant metastasis breast cancer of 21.5% and 38.2%, respectively. Cancer can not be cured and can spread to other parts of the body by blood stream and the lymphatic system. The tumor cell spreading through the blood stream was 60.90% in distant metastasis, and through the lymphatic system 34.8% of distant metastasis breast cancer. For hormone receptor status, estrogen receptor positive had 22.2% of distant metastasis and 17.8% in progesterone receptor positive. The patients with estrogen and progesterone positive receptors tended to have a better prognosis than patients who did not have these receptors[11]. The 21.9% of patients with gene p53 mutation got distant metastasis. The p53 mutation can increase the likelihood for the cell that will begin uncontrolled division[12]. The 21.8% of patients with HER-2 over-expression got distant metastasis. The tumor cell with an abnormally high number of HER-2 gene per cell is called HER-2 protein over-expression. The more HER-2 protein, the more risk that cancer cells can grow and divide more quickly[13].

In binary logistic regression, there were nine prognostic predictors that associated with the occurrence of distant metastasis breast cancer including vascular invasion, histologic grade III, lymphatic invasion, tumor size, estrogen receptor, progesterone receptor, p53, radiation therapy and hormonal therapy. In ordinal logistic regression, it was found that the coefficients(β) had parallel slopes[14]. Order condition of respond variables are least aggressive, mild aggressive, moderate aggressive and severe aggressive. Based on the ordinal logistic regression, there were 8 prognostic predictors including vascular invasion, histologic grade III, lymphatic invasion, tumor size, estrogen receptor, p53, radiation therapy and hormonal therapy.

In this study, the prognostic factor of vascular invasion showed the highest OR. Another group of variables with moderate OR were estrogen receptor, lymphatic invasion, histologic grade III, p53 and tumor size. The adjuvant therapies gave OR<1. A follow up system for those at risk for metastasis is suggested.

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# การค้นหาปัจจัยทำนายการเกิดการลุกลามของโรคมะเร็งเต้านม: ทะเบียนข้อมูลโรคมะเร็ง สถาบันมะเร็งแห่งชาติ

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## บทคัดย่อ

การศึกษาแบบ retrospective cohort ในผู้ป่วยมะเร็งเต้านมที่รับการวินิจฉัยและรักษาที่สถาบันมะเร็งแห่งชาติ พ.ศ 2547 จำนวน 893 ราย เพื่อศึกษาความสัมพันธ์ระหว่างปัจจัยทำนายกับโอกาสในการเกิดการลุกลามไปยังอวัยวะอื่นของผู้ป่วยมะเร็งเต้านม วิเคราะห์ข้อมูลด้วย binary และ ordinal logistic regression models ในช่วง 3 ปีของการศึกษาพบการลุกลามของมะเร็งเต้านม 129(14.45%) ราย ไปที่กระดูกมากที่สุด47.3% การวิเคราะห์ด้วย binary logistic regression พบตัวแปรที่มีความสัมพันธ์กับการลุกลามของโรค คือ vascular invasion (OR = 8.8), histologic grade III (OR = 2.9), lymphatic invasion (OR = 2.4), estrogen receptor (OR = 2.2), progesterone receptor (OR = 2.0), p53 (OR=1.8), tumor size (OR = 1.2), radiation therapy (OR = 0.5) และ hormonal therapy (OR = 0.4) ผู้ป่วยมะเร็งเต้านมจำนวน 75, 28 และ 26 ราย เกิดการลุกลามหลังการวินิจฉัยโรคในปีที่ 1, 2 และ 3 ตามลำดับ การวิเคราะห์ด้วย ordinal logistic regression พบตัวแปรที่มีความสัมพันธ์กับการเกิดการลุกลามของโรคคือ vascular invasion (OR = 5.6), estrogen receptor (OR= 2.3), lymphatic invasion(OR = 2.3), histologic grade III (OR = 1.9), p53 (OR = 2.0), tumor size (OR = 1.2), radiation therapy (OR = 0.6)และ hormonal therapy (OR = 0.5) ทั้งสองโมเดลของสมการถดถอยโลจิสติก ตัวแปรทำนายที่ให้ค่า OR สูงสุดคือ vascular invasion ตัวแปรที่ให้ค่า OR ในระดับปานกลางคือ estrogen receptor, lymphatic invasion, histologic grade III, p53 และ tumor size ตัวแปรที่ให้ค่า OR < 1 คือ adjuvant therapy การวินิจฉัยตัวแปรที่มีความสำคัญและมีค่า OR ที่มีนัยสำคัญกับการลุกลามของโรคจึงเป็นความจำเป็นและควรมีระบบการติดตามในผู้ป่วยมะเร็งเต้านมที่มีความเสี่ยงสูงต่อการเกิดการลุกลามของมะเร็งเต้านม

***คำสำคัญ:*** มะเร็งเต้านม, การลุกลามของมะเร็งเต้านม, ปัจจัยทำนาย

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