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Lampiran 2 surat Pernyataan

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Faktor Klinis dan Histopatologi serta Hubungannya dengan Kekambuhan Pasca-operasi pada Pasien Kanker Payudara di RSUD Dr. Soetomo, Januari–Juni 2015

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Diterima: 7 Februari 2017; Direview: 9 Maret 2017; Disetujui: 23 Juni 2017

ABSTRACT

Breast cancer recurrence occurs because of factors such as surgical problem and clinicopathological features. The present study aimed to assess the relation between clinicopathological factors to breast cancer recurrence. Cross sectional design was used to take medical documents of all patients who visited Out Patient Department Soetomo Hospital from January 2015 to June 2015. A total of 228 patients were identified. The rates of breast cancer recurrence were 30%, most of recurrence occurred in first 5 years and the peak was in the first year. There were significant correlations between breast cancer recurrence and the factors observed below: tumor size ($p=0.01$, PR(95% CI)=1.621(1.086-2.421)); nodal status 1-3 and $\geq 4 \geq 4$ (respectively $p=0.014$, PR(95% CI)=1.281(1.030-2.593); $p=0.011$, PR(95% CI) = 1.289(1.038-1.601)); tumor location ($p=0.00$, PR(95% CI)=2.422(1.576-3.721)); hospital where the operation performed ($p=0.03$, PR(95% CI)=1.207(1.026-1.421)); adjuvant therapy ($p=0.00$, PR(95% CI)= 4.371(2.231-8.566)). However there were no correlations of breast cancer recurrence and age, clinical stage or type of surgery. Conclusion, there are significant correlations between breast cancer recurrence and clinicopathological factors, such as tumor size, nodal status, tumor location, hospital where the operation performed and adjuvant therapy.

Keyword: breast cancer recurrence, clinicopathological factors

ABSTRAK

Kekambuhan kanker payudara terjadi karena beberapa faktor, di antaranya faktor klinis dan histopatologi. Penelitian ini bertujuan untuk mengetahui hubungan faktor klinis dan histopatologi terhadap kekambuhan. Penelitian ini menggunakan desain cross sectional dengan mengambil data dari rekam medis pasien yang berkunjung ke Unit Rawat Jalan RSUD Dr. Soetomo periode Januari–Agustus 2015. Sebanyak 228 pasien diidentifikasi. Tingkat kekambuhan kanker payudara sebesar 30%, sebagian besar kekambuhan terjadi dalam 5 tahun pertama, dan puncaknya adalah pada tahun pertama. Ada hubungan yang signifikan antara kekambuhan kanker payudara dengan faktor-faktor yang diamati: ukuran tumor ($p=0.01$, PR (95%CI) =1.621 (1.086-2.421)); status nodal 1-3 and $\geq 4 \geq 4$ (masing-masing $p=0,014$, PR(95%CI) = 1.281(1.030-2.593); $p=0,011$, PR (95%CI) = 1.289(1.038-1.601)); letak tumor ($p=0,00$, PR(95%CI) = 2.422(1.576-3.721)); rumah sakit tempat operasi dilaksanakan($p=0,03$, PR,(95%CI)=1.207(1.026-1.421)); tetapi adjuvant ($p=0,00$, PR(95%CI)=

Factors affecting local recurrence and distant metastases of invasive breast cancer after breast-conserving surgery in Chiang Mai University Hospital

This article was published in the following Dove Press journal:

Breast Cancer: Targets and Therapy

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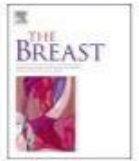
Background: The purpose of this study was to collect data regarding breast cancer profiles and factors that affect local recurrence and distant metastasis after breast-conserving surgery (BCS) in Chiang Mai University Hospital.

Materials and methods: This study was a retrospective review in a single institution of newly diagnosed invasive breast cancer patients who were treated with BCS between April 9, 2001 and December 25, 2011.

Results: A total of 185 patients treated with BCS were included in this study, with an average age of 46.83 years. The average recurrence age was 41.1 years and the average nonrecurrence age was 47.48 years, with a recurrence rate of 10.27%. Premenopause was significant in recurrence ($P=0.047$), as well as non-estrogen-expression patients ($P=0.001$) and patients who did not receive antihormonal treatment ($P=0.011$).

Conclusion: The recurrence rate in our institute was 10.27%. Factors affecting recurrence after BCS included young age, premenopausal status, nonexpression of the estrogen receptor, and patients who had not received antihormonal treatment. The recurrence rate was higher in the first 90 postoperative months.

Keywords: breast-conserving surgery, breast cancer surgery, invasive breast cancer, factor, recurrence



Original article

Effect of multidisciplinary team care on the risk of recurrence in breast cancer patients: A national matched cohort study



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ABSTRACT

Background: Cancer has been the leading cause of death in the past decade in Taiwan, with breast cancer being the most common type of cancer in females. Very few studies looked at the risk of recurrence in patients who received multidisciplinary team (MDT) care. We analyzed the influence of MDT on the risk of recurrence and death in breast cancer patients.

Method: In this retrospective study, we included newly diagnosed patients from 2004 to 2010. The study included 9,266 breast cancer patients who were enrolled in MDT care and 9,266 patients who were not. The study used log-rank test to analyze patients' characteristics, hospital characteristics, cancer staging, and treatment methods to compare the recurrence rates in MDT care and non-MDT care participants. We used Cox proportional hazards model to examine the effect of MDT and associated factors on the risk of recurrence and mortality of breast cancer patients.

Results: Relative risk of recurrence was lower for patients who received MDT care than for patients who did not (HR, 0.84; 95%CI: 0.70–0.99) after matching. The mortality risk for breast cancer patients with relapse was 8.48 times (95%CI: 7.53–9.54) than that for patients without relapse.

Conclusions: The relative risk of recurrence and death was significantly lower for breast cancer patients who received MDT care than for those who did not. We suggest that MDT care be implanted in the National Health Policy settings of breast cancer patients.

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Annual Hazard Rates of Recurrence for Breast Cancer During 24 Years of Follow-Up: Results From the International Breast Cancer Study Group Trials I to V

Marco Colleoni, Zhuoxin Sun, Karen N. Price, Per Karlsson, John F. Forbes, Beat Thürlimann, Lorenzo Gianni, Monica Castiglione, Richard D. Gelber, Alan S. Coates, and Aron Goldhirsch

See accompanying editorial on page 895

Marco Colleoni and Aron Goldhirsch, European Institute of Oncology and International Breast Cancer Study Group, Milan; Lorenzo Gianni, Ospedale degli Infermi and Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori, Rimini, Italy; Zhuoxin Sun, Karen N. Price, and Richard D. Gelber, International Breast Cancer Study Group Statistical Center and Frontier Science and Technology Research Foundation; Zhuoxin Sun and Richard D. Gelber, Harvard T.F. Chan School of Public Health; Richard D. Gelber, Dana-Farber Cancer Institute and Harvard Medical School, Boston, MA; Per Karlsson, Institute of Selected Clinical Sciences, Sahlgrenska Academy, Sahlgrenska University Hospital, Gothenburg, Sweden; John F. Forbes, Australia and New Zealand Breast Cancer Trials Group, University of Newcastle, Newcastle Mater Hospital, Newcastle; Alan S. Coates, International Breast Cancer Study Group and University of Sydney, Sydney, New South Wales, Australia; Beat Thürlimann, Breast Center Kantonsspital, St Gallen, and Swiss Group for Clinical Cancer Research; and Monica Castiglione, International Breast Cancer Study Group, Bern, Switzerland.

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A B S T R A C T

Purpose

Predicting the pattern of recurrence can aid in the development of targeted surveillance and treatment strategies. We identified patient populations that remain at risk for an event at a median follow-up of 24 years from the diagnosis of operable breast cancer.

Patients and Methods

International Breast Cancer Study Group clinical trials I to V randomly assigned 4,105 patients between 1978 and 1985. Annualized hazards were estimated for breast cancer-free interval (primary end point), disease-free survival, and overall survival.

Results

For the entire group, the annualized hazard of recurrence was highest during the first 5 years (10.4%), with a peak between years 1 and 2 (15.2%). During the first 5 years, patients with estrogen receptor (ER) – positive disease had a lower annualized hazard compared with those with ER-negative disease (9.9% v 11.5%; $P = .01$). However, beyond 5 years, patients with ER-positive disease had higher hazards (5 to 10 years: 5.4% v 3.3%; 10 to 15 years: 2.9% v 1.3%; 15 to 20 years: 2.8% v 1.2%; and 20 to 25 years: 1.3% v 1.4%; $P < .001$). Among patients with ER-positive disease, annualized hazards of recurrence remained elevated and fairly stable beyond 10 years, even for those with no axillary involvement (2.0%, 2.1%, and 1.1% for years 10 to 15, 15 to 20, and 20 to 25, respectively) and for those with one to three positive nodes (3.0%, 3.5%, and 1.5%, respectively).

Conclusion

Patients with ER-positive breast cancer maintain a significant recurrence rate during extended follow up. Strategies for follow up and treatments to prevent recurrences may be most efficiently applied and studied in patients with ER-positive disease followed for a long period of time.

SCIENTIFIC REPORTS

OPEN

The association of young age with local recurrence in women with early-stage breast cancer after breast-conserving therapy: a meta-analysis

Received: 10 March 2017

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Xiang-Ming He & De-Hong Zou

The aim of this meta-analysis is to determine the relationship between young age and local recurrence in patients with early-stage breast cancer after breast-conserving therapy. Eligible studies were retrieved from various electronic databases. Among the 19 studies included, 14 studies were analyzed for 5-year local recurrence rate and 8 studies for 10-year local recurrence rate using random effects models. Both results showed that young patients were at higher risk of local recurrence compared to old patients (5-year: RR = 2.64, 95% CI (1.94–3.60); 10-year: RR = 2.37, 95% CI (1.57–3.58)). Harbord's modified test showed the presence of publication bias in both 5- and 10-year local recurrence rates ($P = 0.019$ and $P = 0.01$, respectively). While the Trim and Fill analysis showed that the presence of publication bias did not affect the overall outcome of the 5-year local recurrence rate (RR = 2.21, 95% CI (1.62, 3.02)), it significantly affected the effect size of the 10-year local recurrence rate (RR = 1.47, 95% CI (0.96, 2.27)). Young age is a significant risk factor for local recurrence developed within 5 years of breast-conserving therapy in patients with early-stage breast cancer. Further high-quality studies are needed to elucidate the relationship between young age and the risk of local recurrence developed within 10 years.

Breast cancer is a systemic malignant disease that can severely threaten a woman's health. Because micrometastasis can be found during the early stages of this disease, comprehensive treatments including surgery, chemotherapy, hormonal therapy, radiotherapy, immunotherapy, and targeted therapy are necessary. Modified radical mastectomy with the retention of the nipple-areola complex originated in the 1970s in Europe and the United States. Now, breast-conserving therapy has become a standard treatment for stage I and stage II breast cancer in

RESEARCH

Open Access

The impact of age on the risk of ipsilateral breast tumor recurrence after breast-conserving therapy in breast cancer patients with a > 5 mm margin treated without boost irradiation



Yuka Ono¹, Michio Yoshimura^{1*}, Kimiko Hirata^{1,2}, Chikako Yamauchi^{1,3}, Masakazu Toi⁴, Eiji Suzuki⁴, Masahiro Takada⁴, Masahiro Hiraoka^{1,5} and Takashi Mizowaki¹

Abstract

Background: The boost irradiation to the tumor bed following whole-breast irradiation (WBI) reduced the risk of ipsilateral breast tumor recurrence (IBTR). However, in Japan, almost all patients with a margin ≤ 5 mm receive boost irradiation to the tumor bed, but the decision to perform boost irradiation for those with a margin > 5 mm is dependent on the institution. Thus, institutional guidelines on utilizing boost irradiation for patients aged ≤ 40 or ≤ 50 years vary. We investigated the IBTR rate to assess the appropriate age for boost irradiation to the tumor bed with a margin > 5 mm.

Methods: From January 1993 to December 2010, 419 patients with early-stage breast cancer and negative margins (> 5 mm) after breast-conserving surgery received WBI without boost irradiation. The Gray test was used to compare the cumulative incidence of IBTR among patients aged ≤ 40 , 41–50, and ≥ 51 years. Hazard ratios were estimated using the Fine and Gray models. Furthermore, as a subgroup analysis, we investigated whether IBTR depended on the use of systemic therapy, such as anthracycline or taxane regimens.





Results: The median follow-up time was 9.3 years. In multivariate analysis, only age predicted IBTR ($p = 0.047$). The 10-year IBTR rate was 15.7% in patients aged ≤ 40 , 3.8% in those aged 41–50, and 2.0% in patients aged ≥ 51 years. The difference between patients aged ≤ 40 and 41–50 years was statistically significant ($p = 0.045$), whereas the difference between patients aged 41–50 and ≥ 51 years was not significant ($p = 0.21$).

Conclusions: In our institutional surgical setting, when boost irradiation is performed only for patients with a margin ≤ 5





Original Research

Recurrence dynamics of breast cancer according to baseline body mass index ☆

[Elia Biganzoli](#)^{a,1}  , [Christine Desmedt](#)^{b,1}  , [Marco Fornili](#)^a,
[Evandro de Azambuja](#)^c, [Nathalie Cornez](#)^d, [Fernand Ries](#)^e, [Marie-Thérèse Closon-Dejardin](#)^f,
[Joseph Kerger](#)^c, [Christian Focan](#)^g, [Angelo Di Leo](#)^h, [Jean-Marie Nogaret](#)ⁱ,
[Christos Sotiriou](#)^b, [Martine Piccart](#)^c, [Romano Demicheli](#)^a

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RESEARCH ARTICLE

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Impact of obesity on breast cancer recurrence and minimal residual disease



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Abstract

Background: Obesity is associated with an increased risk of breast cancer recurrence and cancer death. Recurrent cancers arise from the pool of residual tumor cells, or minimal residual disease (MRD), that survives primary treatment and persists in the host. Whether the association of obesity with recurrence risk is causal is unknown, and the impact of obesity on MRD and breast cancer recurrence has not been reported in humans or in animal models.

Methods: Doxycycline-inducible primary mammary tumors were generated in intact *MMTV-rtTA;TetO-HER2/neu* (*MTB/TAN*) mice or orthotopic recipients fed a high-fat diet (HFD; 60% kcal from fat) or a control low-fat diet (LFD; 10% kcal from fat). Following oncogene downregulation and tumor regression, mice were followed for clinical recurrence. Body weight was measured twice weekly and used to segregate HFD mice into obese (i.e., responders) and lean (i.e., nonresponders) study arms, and obesity was correlated with body fat percentage, glucose tolerance (measured using intraperitoneal glucose tolerance tests), serum biomarkers (measured by enzyme-linked immunosorbent assay), and tissue transcriptomics (assessed by RNA sequencing). MRD was quantified by droplet digital PCR.

Results: HFD-Obese mice weighed significantly more than HFD-Lean and LFD control mice ($p < 0.001$) and had increased body fat percentage ($p < 0.001$). Obese mice exhibited fasting hyperglycemia, hyperinsulinemia, and impaired glucose tolerance, as well as decreased serum levels of adiponectin and increased levels of leptin, resistin, and insulin-like growth factor 1. Tumor recurrence was accelerated in HFD-Obese mice compared with HFD-Lean and LFD control mice (median relapse-free survival 53.0 days vs. 87.0 days vs. 80.0 days, log-rank $p < 0.001$; HFD-Obese compared with HFD-Lean HR 2.52, 95% CI 1.52–4.16; HFD-Obese compared with LFD HR 2.27, 95% CI 1.42–3.63). HFD-Obese mice harbored a significantly greater number of residual tumor cells than HFD-Lean and LFD mice ($12,550 \pm 991$ vs. $7,339 \pm 2,182$ vs. $4,793 \pm 1,618$ cells, $p < 0.001$).

Conclusion: These studies provide a genetically engineered mouse model for study of the association of diet-induced

RESEARCH

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Factors that predict recurrence later than 5 years after initial treatment in operable breast cancer

Pattaraporn Wangchinda and Suthinee Ithimakin*

Abstract

Background: Occasionally, breast cancer relapses more than 5 years after initial treatment, sometimes with highly aggressive disease in such late-recurring patients. This study investigated predictors of recurrence after more than 5 years in operable breast cancer.

Methods: We retrospectively analyzed data from patients with recurrent breast cancer treated at Siriraj Hospital. Patients were divided into those whose relapse times were longer or shorter than 5 years. Factors that predicted late recurrence were analyzed in both the overall population and the luminal subgroup. Patterns of relapse, changes in biomarkers, and time to disease progression after first relapse were also recorded.

Results: We included 300 women whose breast cancers recurred between 2005 and 2013, of whom 180 had recurrence within 5 years of diagnosis and 120 later than 5 years (median time to recurrence: 45.43 months; range: 4.4–250.3 months). Tumors larger than 2 cm, lymph node metastasis, and high nuclear grade were related with early recurrence. Estrogen receptor-positive, progesterone receptor-positive, and HER2⁻ disease predicted late recurrence. Almost all late-relapsing patients with luminal tumors had high estrogen receptor (ER⁺) titers ($\geq 50\%$) and HER2⁻ disease. Liver and brain were the most common early recurrence sites. Biomarkers did not significantly change by time of recurrence.

Conclusions: ER⁺/PR⁺ and HER2⁻ patients have higher risk of recurrence later than 5 years, especially in patients with high ER titer and low nuclear grade. Larger and node-positive tumors had higher risk of early recurrence.

Keywords: Breast cancer, Clinicopathological, Late recurrence, Luminal breast cancer

Abbreviations: ER, Estrogen receptor; HER2, Human epidermal receptor 2; TN, Triple-negative; PR, Progesterone receptor; ICD10, International classification of disease and related health problem 10th revision; DFS, Disease-free

RESEARCH ARTICLE

Open Access



Factors associated with late recurrence after completion of 5-year adjuvant tamoxifen in estrogen receptor positive breast cancer

Eun-Shin Lee¹, Wonshik Han^{1,6*}, Min Kyoon Kim², Jongjin Kim³, Tae-kyung Yoo¹, Moo Hyun Lee⁴, Kyung Hun Lee⁵, Tae Yong Kim⁵, Hyeong-Gon Moon⁵, Seock-Ah Im⁵, Dong-Young Noh¹ and Eun Sook Lee⁴

Abstract

Background: Recent large trials have shown the survival benefits of 10-year use of tamoxifen by reducing late recurrence compared with 5-year therapy in estrogen receptor(ER)-positive breast cancer. We tried to identify clinical factors associated with the late recurrence.

Methods: We reviewed our database of ER-positive patients who had received operations between 1996 and 2006 in two institutions. We selected 444 who had completed 5-year tamoxifen and were disease-free up to 10 years after the operation. Patients who had received aromatase inhibitors with any regimens were excluded. As a late recurrence group, 139 patients were identified who had completed 5-year tamoxifen, but had recurrence afterwards. Among them, 61 had local/contralateral breast recurrence and 78 had distant metastasis. The median follow-up was 9.7 years. Clinicopathological factors at the time of initial operation, such as age, menopausal status, progesterone receptor expression, HER2 status, tumor grade and Ki-67, were compared between the disease-free group and the late recurrence group.



Results: In a univariate analysis, tumor size (>2 cm), lymph node metastasis and high histologic grade were significantly associated with late recurrences ($p < 0.05$). In a multivariate analysis, only axillary lymph node metastasis was significant ($p < 0.001$). Late distant metastasis was significantly associated with tumor size and axillary lymph node metastasis ($p = 0.038$, $p < 0.001$, respectively). Late local/contralateral breast recurrence was associated with axillary lymph node metastasis ($p = 0.042$).







Conclusions: Our data showed axillary lymph node metastasis at initial operation was the only risk factor of late




Lampiran 4 Lembar Konsultasi



KARTU BIMBINGAN SKRIPSI

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 Pembimbing : Apt. Rizki Nur Azmi, M.Farm

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2	Sabtu 27 November 2021	Bab 1, 2, dan 3	<ul style="list-style-type: none"> - Perubahan judul - Tambahkan latar belakang - Et.al huruf italic - Rumusan masalah dan tujuan dibuat per poin. 	Herdiana	

No	Tanggal	Materi Bimbingan	Arahan/ Masukan	Paraf	
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3	Setelah 7 Desember 2021	Bab 1,2 dan 3	Acc Proposal Skripsi		
4	4/07/2022	Bab 3,4,5	Menambahkan jurnal hasil Penelitian		
5	6/07/2022	Bab 4	Revisi hasil Penelitian		

No	Tanggal	Materi Bimbingan	Arahan/ Masukan	Paraf	
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6	10/08/2022	Revisi bab 3 dan 4	Mengubah rumusan masalah dan Menambahkan gambar alur penelitian	Huf	
7	16/08/2022	Revisi Bab IV	Menambahkan Penjelasan hasil Penelitian	Huf	
8	21/12/2022	Revisi Bab IV dan V	Menambahkan Usia, ER, BMI dan ukuran tumor	Huf	

No	Tanggal	Materi Bimbingan	Arahan/Masukan	Paraf	
				Mahasiswa	Dosen
9	4/01/2023	Revisi seluruh bab	Menambahkan Permasalahan Penelitian Membuat tabel hitung	Haf	
10	Jumat 6 Januari 2023	Bab 1,2,3,4 dan 5	ACC Skripsi	Haf	

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