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HASIL PENILAIAN SEJAWAT SEBIDANG ATAU PEER REVIEW
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Judul Karya Ilmiah (Artikel) : BRCA1 Gene Mutation Screening for the Hereditary Breast and/or Ovarian Cancer Syndrome in Breast Cancer Cases: a First High Resolution DNA Melting Analysis in Indonesia

Jumlah Penulis : 4 Orang

Status Pengusul : Farmaditya EP Mundhofir, Catharina EndahWulandari, Yan Wisnu Prajoko, Tri Indah Winarni

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i. Terindeks di : Q2 SJR 0,5, H Index 70

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Semarang, 13 Februari 2021

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BRCA1 gene mutation screening for the Hereditary Breast and/or Ovarian cancer syndrome in breast cancer cases: A first high resolution DNA melting analysis in Indonesia

Mundhofir F.E.P.^a , Wulandari C.E.^a, Prajoko Y.W.^b, Winarni T.I.^a

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Abstract

Specific patterns of the hereditary breast and ovarian cancer (HBOC) syndrome are related to mutations in the BRCA1 gene. One hundred unrelated breast cancer patients were interviewed to obtain clinical symptoms and signs, pedigree and familial history of HBOC syndrome related cancer. Subsequently, data were calculated using the Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm (BOADICEA) risk prediction model. Patients with high score of BOADICEA were offered genetic testing. Eleven patients with high score of BOADICEA, 2 patients with low score of BOADICEA, 2 patient's family members and 15 controls underwent BRCA1 genetic testing. Mutation screening using PCR-HRM was

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Mutations analysis of BRCA1 gene in patients with breast cancer in South Khorasan province, East Iran

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carried out in 22 exons (41 amplicons) of BRCA1 gene. Sanger sequencing was subjected in all samples with aberrant graph. This study identified 10 variants in the BRCA1 gene, consisting of 6 missense mutations (c.1480C>A, c.2612C>T, c.2566T>C, c.3113A>G, c.3548 A>G, c.4837 A>G), 3 synonymous mutations (c.2082 C>T, c.2311 T>C and c.4308T>C) and one intronic mutation (c.134+35 G>T). All variants tend to be polymorphisms and unclassified variants. However, no known pathogenic mutations were found.

Author keywords

BOADICEA; BRCA1 gene; HBOC syndrome; Indonesian population; PCR-HRM

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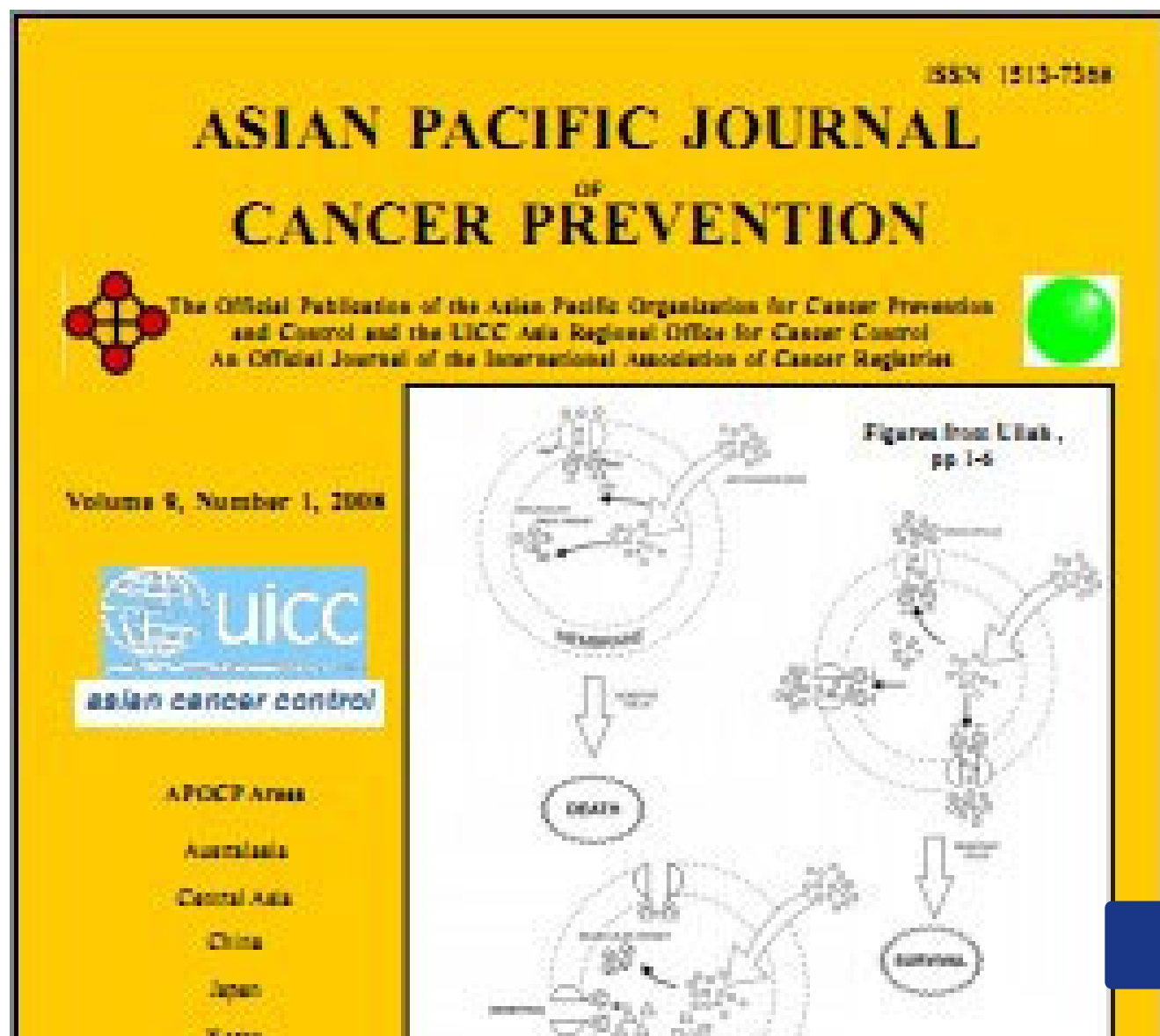
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RESEARCH ARTICLE

Hormone Use is Associated with Lymphovascular Invasion in Breast Cancer

Margaretha Loof-Johanson^{1*}, Lars Brudin^{1,2}, Marie Sundquist³, Carl Edvard Rudebeck⁴

Abstract

Background: Risk of developing breast cancer increases with short breastfeeding and the use of hormones. The prognosis of breast cancer is better if the tumours are hormone receptor positive. Since breast feeding affects estrogen and progesterone receptors, we wanted to investigate how such reproductive factors as breastfeeding and the use of hormones interact with known prognostic markers and specific tumour characteristics in women with breast cancer. **Materials and Methods:** A total of 250 women treated for breast cancer from a larger cohort completed a questionnaire on breastfeeding, number and age at births and use of hormones. A logistic regression analysis was made to search for connections between known prognostic markers on the one hand (type of cancer, grade, tumor size, estrogen receptor and progesterone receptor, lymphovascular invasion and DNA-ploidy) and reproductive data, breastfeeding, and hormone use on the other. **Results and Conclusions:** Hormone use, but not breastfeeding, was significantly associated, also on multivariate analysis, with the prognostic variable lymphovascular invasion, connected to a worse prognosis. No other hormone use or breast feeding correlations with prognostic variables were found.

Keywords: Breastfeeding - childbirth - breast cancer - prognostic factors in breast cancer - LVI - NHG - DNA - ER/PR

Asian Pac J Cancer Prev, 17 (3), 1507-1512

Introduction

Risk of developing breast cancer increases with short breastfeeding and use of hormones (Collaborative Group on Hormonal Factors in Breast Cancer 2002; Anothaisintawee et al., 2013; Antoine et al., 2014; Schneider et al., 2014). Anothaisintawee et al., 2013 assumed that the etiology of breast cancer can be explained by two mechanisms of differentiation and proliferation of breast epithelial cells mediated by hormonal factors. They found associated adverse risk factors for both mechanisms in the use of oral contraceptives (OC) and hormonal replacement therapy (HRT). The association with breastfeeding as a significant and positive influence factor against breast cancer decreased the risk with 28% if breastfeeding ≥ 12 months.

Li et al. found, 2013 that breastfeeding generates a lower risk of triple-negative breast cancer, (TNBC=negative ER/PR and Her2 breast cancer) supported by both their case-control studies ($p=0.02$) and case-case comparisons ($p=0.01$). Their observations are consistent with the results of the majority of studies that have assessed these relationships and breastfeeding is the most consistently identified factor to be differentially associated with risk of triple- negative cancer compared to other major molecular

subtypes of the disease. The biological mechanisms for this is largely unknown.

Phipps et al., 2011, present different results. They found that nulliparity was associated with decreased risk of triple-negative breast cancer but increased risk of ER+ breast cancer. Among parous women, the number of births was positively associated with risk of triple-negative disease for three births or more vs one birth- and inversely associated with risk of ER+ disease. Ages at menarche and menopause were modestly associated with risk of ER+ but not triple-negative breast cancer; breastfeeding and oral contraceptive use were not associated with either subtype.

Work et al. assume, 2014, that the ER / PR negative breast cancer has a poorer prognosis compared with other subtypes of breast cancer and that breast-feeding >12 months can reduce the risk of all subtypes and with the strongest effect on ER- / PR-.

Our knowledge of how reproductive factors and the use of hormones affect the risk of developing breast cancer is greater than our knowledge of how the prognosis of the breast cancer is affected. Here we have a large need for research (Kwan et al., 2015).

Our aim was to evaluate if reproductive factors or use of hormones were associated with any specific tumour characteristics. Since breast feeding and the use of

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RESEARCH ARTICLE

Prognostic Factors and Survival in Acute Myeloid Leukemia Cases: a Report from the Northeast of Iran

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Abstract

Background: Acute myeloid leukemia (AML) is a clonal hematopoietic disorder resulting from genetic alterations in normal hematopoietic stem cells. The aim of this study was to evaluate prognostic factors and survival of AML patients in the Northeast of Iran. **Materials and Methods:** This retrospective study covered 96 patients with AML referred to Emam Reza Hospital, Mashhad city, Iran, from 2009 to 2015. Age, sex, blood group, type of AML, fever, consumption of amphotericin B, cytogenetic forms and survival were analyzed. Also, WBC, hemoglobin and platelet levels were checked. Mean follow-up was 30.5 months (60.4% mortality). Survival was plotted by GraphPad Prism 5 with Log-rank test. **Results:** The mean age for all AML patients at diagnosis was 40.4 years (range, 17-77 years). Some 42.7% patients were aged <35 years and 40.6% were male. In all patients, 76% had fever and 50% consumed amphotericin. T(15;17)(q22;q21) had the most prevalence (37.7%) compared to other forms. Out of 92 patients, O+(30.4%) was the most common blood group and AML-M5 (28.3%) the most common subtype. There was a significant difference in survival based on WBC and consumption of amphotericin B ($P<0.05$). **Conclusions:** WBC level, fever and consumption of amphotericin B proved to be factors for survival of AML patients. The mean age for patients in Iran is lower than other areas in the World and also survival in this study was higher than in other studies.

Keywords: AML - survival - amphotericin B - WBC - northeastern Iran

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Introduction

Acute myeloid leukemia (AML) in adults is the most common malignant myeloid disorder and this disease is a heterogeneous clonal disorder of hemopoietic (blood-forming) progenitor cells. The median age at diagnosis for patients with AML is 70 years (Estey and Döhner, 2006). The etiology of AML is not well understood (Strom et al., 2012). A number of factors have been reported as affecting the outcome of the disease such as age, White Blood Cell (WBC) count in diagnosis, time to achieve complete remission, abnormal karyotypes and cytogenetics (Ayremlou et al., 2012). Cytogenetic analysis at the time of diagnosis is among the most important independent prognostic factors in patients with AML (Mrozek, 2008). The chromosomal abnormalities such as t(8;21) (q22;q22), t(16;16) (p13;q22), and t(15;17) (q22;q21) have a good prognosis (Mazloumi et al., 2012). The prognosis of elderly patients with AML is usually dismal, while the true survival of older patients not included in clinical trials is not known (Pulsoni et al., 2004). Advances in understanding of the pathophysiology of AML have not yet led to major improvements in overall survival of adults

with this disease (Stone et al., 2004). AML is divided into subgroups that are distinguished by the morphology of the leukemia cells, specific chromosomal abnormalities, gene rearrangement patterns, and different clinical courses and response to therapy (Douer, 2003). AML is subdivided based on morphologic criteria by the French-American-British (FAB) classification (Walter et al., 2013). FAB group has classified AML cases into eight subgroups (M0-M7) (Ziaei, 2004). National and international studies have reported AML-M2 as the predominant FAB subtype of AML (Harani et al., 2005). More patients with AML are presented with fever (over 50%) (Hassan et al., 1993). Because of the increasing prevalence and changing microbiological spectrum of invasive fungal infections, some form of amphotericin B still provides dependable and broad spectrum therapeutic alternative (Hamill, 2013). Invasive fungal diseases cause morbidity and mortality in patients with AML (Girmenia et al., 2012). Amphotericin B associates with reducing of neutropenic fever in the majority of patients (Spitzer et al., 1989).

The aim of this study is to evaluate prognostic factors and affecting of them on survival in AML patients in the in the Northeast of Iran

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