

ER, PR, AND HER-2/NEU PROFILE ON YOUNG BREAST CARCINOMA PATIENTS

Caesarisma Vidiyanti¹, Dyah Fauziah², Desak Gede Agung Suprabawati³

¹Medical Education Program, ²Department of Anatomic Pathology, ³Department of Surgery
Faculty of Medicine, Airlangga University, Surabaya

ABSTRAK

Kanker payudara merupakan salah satu keganasan terbanyak pada wanita dengan kecenderungan meningkat tiap tahunnya. Bukti-bukti kuat menunjukkan kecenderungan kanker terjadi pada usia yang lebih muda. Tujuan penelitian ini adalah mengamati karakteristik estrogen reseptor (ER), progesteron reseptor (PR), dan HER-2/neu pada wanita penderita karsinoma payudara usia muda sepanjang tahun 2010. Status ER, PR dan HER-2/neu didapatkan dari Departemen/SMF/Instalasi Patologi Anatomi FK UNAIR/RSUD Dr. Soetomo Surabaya selama 2010, dengan data-data terkait yang didokumentasikan. Hanya rekam medis kanker payudara dengan status ER, PR dan HER-2/neu dan usia kurang dari atau sama dengan 35 tahun yang diambil sebagai sampel. Dari 21 kasus, usia berkisar dari 26 hingga 35 tahun dengan median 32 tahun, dimana kasus paling umum terjadi pada usia 35 tahun. Status ER positif ditemukan pada 42.86% sampel, PR positif pada 19.05% sampel, dan HER-2/neu ekspresi positif pada 33.34% sampel. Sebagian besar pasien memiliki status ER negative, status PR negative, dan status HER-2/neu negatif. Dibutuhkan pemeriksaan lebih lanjut dengan fluorescence in situ hybridization (FISH). (FMI 2014;50:15-18)

Kata kunci: Kanker Payudara, Reseptor Estrogen, Reseptor Progesteron, HER-2/neu

ABSTRACT

Breast carcinoma is one of the most common malignancy in women with increasing incidence rate every year. Evidence strongly suggested the cancer tends to occur at younger age. The aim of this study is to observe the characteristic of estrogen receptor (ER), progesterone receptor (PR), and HER-2/neu in young female breast carcinoma patient during 2010. ER, PR and HER-2/neu status were obtained from Pathology Anatomy Department Faculty of Medicine Airlangga University/Dr. Soetomo Hospital medical records throughout 2010, with related data documented. From the medical records, only breast carcinoma with available ER, PR and HER-2/neu status with age of patient less or equal to 35 years old were taken as samples. From 21 cases, the age ranged from 26 to 35 years old, with median of 32 years old and the most common age was 35 years old. ER status was positive in 42.86% samples, PR status was positive in 19.05% samples and HER-2/neu expression was positive on 33.34% samples. Most patient have negative ER status, negative PR status, and negative HER-2/neu expression. Further examination with fluorescence in situ hybridization (FISH) is required. (FMI 2014;50:15-18)

Keywords: breast carcinoma, estrogen receptor, progesterone receptor, HER-2/neu

Correspondence: Caesarisma Vidiyanti, Medical Education Program, Faculty of Medicine, Airlangga University, Surabaya

INTRODUCTION

Currently, breast cancer is a malignancy suffered by female with increasing incidence rate every year (Sadhana 2007). Statistics from WHO shows the incidence rate of breast cancer reached seven million people a year, while mortality rate is up to five million people (Ministry of Health, Republic of Indonesia 2008). High risk group of breast cancer is 35-64 years old individuals, peaking at 34-44 years old. Based on St. Gallen Guidelines supported by American Society of Clinical Oncology, young criteria in breast cancer patient is less or equal to 35 years old (Avis et al 2005). Breast cancer cases on young female patients (≤ 35 years old) in 2002-2006 amount to 26.9% of total breast malignancy (Kartika et al 2009).

Breast cancer rarely occurs on patients younger than 30 years old, after which the risk increases with age, until after menopause the curve is almost horizontal (Kumar et al 2002). Compared to sporadic cancer which usually appear after age 50, hereditary cancer tends to appear at many younger patients. This is due to the nature in hereditary cancer patients, where an allele is already damaged, leading to only one healthy allele remains, while in sporadic cancer patients both alleles are originally healthy. Once both alleles are defective, carcinoma will occur (Purnomosari 2007).

A reason to high rate of breast malignancy on younger patients is the difficulties to detect breast cancer, where their breast tissues are generally denser compared to older patients. Additionally, breast cancer on young patients is more aggressive and harder in response to the

therapy (Chang 2009). This leads to a high rate of patients with advanced stage of breast cancer, reaching 70-90% of patients treated in hospital (Tjindarbumi 1982), where the therapy is harder and the result tends to be unsatisfying. Meanwhile on early stage of breast cancer, the recovery rate is 75% (Ama 1990).

Aggressiveness of breast cancer is influenced by hormones, mainly estrogen and progesterone. In addition to hormones, HER-2/neu gene affects breast carcinoma as a gene for signaling cell growth, reproduction and repair. The goal of this study is to outline estrogen receptor (ER), progesterone receptor (PR) and HER-2/neu profile in young female breast cancer patients, as well as providing scientific information for basis of treatment on breast cancer in the group aforementioned.

MATERIALS AND METHODS

The study was descriptive with cross sectional design. Samples were taken from medical records of all breast carcinoma patient in Pathology Anatomy Department Faculty of Medicine Airlangga University/Dr. Soetomo Hospital based on paraffin block with immunohistochemistry coloration performed using antibody against estrogen receptor (ER), progesterone receptor (PR), and HER-2/neu during 2010. Inclusion criteria was the patient is less or equal to 35 years old. Input from medical records was screened with inclusion criteria of patient younger or equal to 35 years old. Status of ER, PR and HER-2/neu was documented. The data is then submitted to frequency distribution table and percentaged. Afterwards the percentage result was presented as bar chart.

RESULTS

Based on the data collected from Pathology Anatomy Department Faculty of Medicine Airlangga University/Dr. Soetomo Hospital, 21 samples were taken after screened with inclusion criteria of the patient is less or equal to 35 years old between January 1, 2010 to December 31, 2010. The range of age was spread between 26 years old to 35 years old, with mean of 32 years old. The modus was 35 years old (4 patients).

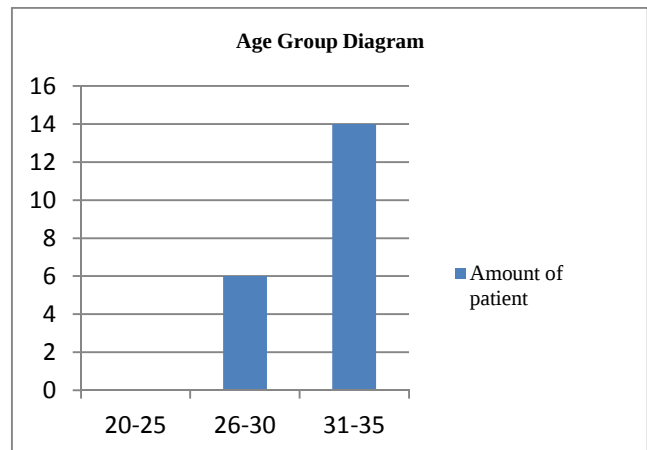


Figure 1. Distribution of samples based on age group

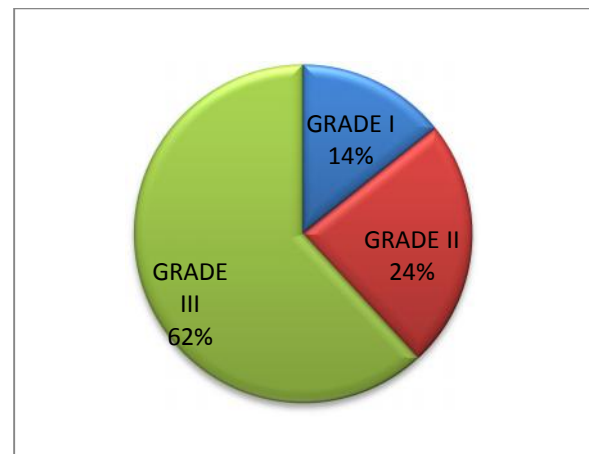


Figure 2. Distribution of samples based on carcinoma grade

From the data of 21 patients of young breast female carcinoma patient obtained, 3 patients suffered from grade 1 carcinoma, 5 patients suffered from grade 2 carcinoma, and 13 patients suffered from grade 3 carcinoma. From the data of hormonal receptor examination, 12 patients were ER negative (57.14%), and 9 patients were ER positive (42.86%). From the data of immunohistochemistry examination for progesterone receptor, 4 patients were PR positive (19.05%) and 17 patients were PR negative (82.61%). Meanwhile from the data of HER-2/neu examination, HER-2/neu gene was not expressed on 12 patients (57.14%), expressed on 7 patients (33.34%), and in 2 patients (9.52%) the HER-2/neu gene was expressed equivocal, where the immunohistochemistry image were positive 2, which needs fluorescence in situ hybridization (FISH) to determine whether the HER-2/neu gene expression is positive or negative.

DISCUSSION

This study was a descriptive study. The data of samples were obtained from Pathology Anatomy Department Faculty of Medicine Airlangga University/Dr. Soetomo Hospital between January 1st 2010 to December 31st 2010 with inclusion criteria of female breast carcinoma patient aged less or equal to 35 years old. From the result obtained, it was concluded that on young female breast carcinoma patient, most suffered from grade 3 carcinoma, most were found to be ER negative, PR negative, and the HER-2/neu gene was mostly not expressed. Hormonal receptor is determined as negative when the concentration is lower than 10%.

In one study, from 55 samples aged 30-34 years old, 15 were positive, 33 were negative, 2 were borderline/equivocal, and 5 were unknown. Borderline/ equivocal estrogen receptor has the same clinical expression as carcinoma with ER negative. The result of our study matched, where most young female breast carcinoma patient has ER negative status. ER status is an important predictor for endocrine therapy response (Sadhana 2007). This also matched with the result of the study, where most young female breast carcinoma patient does not respond positively to endocrine therapy.

Most of the young female breast cancer patient on our study categorized as progesterone receptor negative. Another study showed that most young patient are progesterone receptor negative. Hormonal receptor (estrogen and progesterone) is more often to be found at low grade breast carcinoma or older patients. A study by Ellis et al (2003) stated carcinoma with ER and PR negative status is associated with bad prognosis, relatively young patient, and higher grade of carcinoma.

HER-2/neu overexpression is stated as positive when intense and complete membrane staining is observed on 10% or more of carcinoma cells. On our study, the samples detected as HER-2/neu positive are 33.34%, HER-2/neu negative are 57.14%, and equivocal samples are 9.52%. A FISH test is required to determine whether the equivocal sample is actually positive or negative. Positive HER-2/neu is associated with bad differentiation, metastasis to lymph node, recurrence and high mortality rate, resulting in bad prognosis (Payne et al 2008), which also supported by another study by Ross et al (2003) which stated the bad prognosis of HER-2/neu overexpression. As most of our samples shows negative HER-2/neu overexpression, it can be assumed that there is no metastasis to lymph nodes yet, low recurrence and mortality rate.

Fisher et al (1980) found a meaningful link between age and hormonal status, where an older patient tends to

have higher chance of positive hormonal receptor. A connection between the menopause status and the onset of breast carcinoma is suspected. On young patients, the fewer estrogen receptors is presumed to be a reaction to the high estrogen level on body circulation, where a pre-menopause patient has 100-500 µg/day while menopause patient estrogen level is 15 µg/day (Fisher et al 1980).

Literature mentioned the tendency of less HER-2/neu overexpression on old age, contrary to the tendency of increasing hormonal receptor. This can be explained as correlation of HER-2/neu with other prognostic factor is a reverse to ER status. It is suspected that a large reduction of ER and PR level explained the clinical resistance of the carcinoma to selective estrogen receptor modulator such as Tamoxifen. Another analysis concluded that carcinoma on young female has low ER and PR positive and high HER-2/neu overexpression, although our study shows a different result for HER-2/neu overexpression. All the study supported the concept of different biological characteristic of carcinoma on young female compared to older female, with tendency to be invasive and unsatisfying biological sign. Breast carcinoma on young patient tends to have higher grade, negative hormonal receptor, bad differentiation, aneuploidy and high S fraction, abnormal p53 expression, greater invasion extension to lymphovascular and overexpression of HER-2/neu compared to carcinoma on older patient.

Limitation of the study includes the state of equivocal samples which requires a more extensive examination, a need for advanced study about ER, PR and HER-2/neu profile on young female breast carcinoma patient and the comparison to old female breast carcinoma patient, and the lack of samples. Additionally, studies to determine the appropriate therapy other than endocrine therapy for young female breast carcinoma patient is essential.

CONCLUSION

Based on our study about estrogen receptor (ER), progesterone receptor (PR), and HER-2/neu profile on young female breast carcinoma patient, it can be settled that on young female breast carcinoma patient, the estrogen receptor tends to be negative, the progesterone receptor tends to be negative, negative HER-2/neu status is more common, negative reaction to endocrine therapy, tendency to suffer from higher grade of carcinoma, good differentiation without metastasis to lymph nodes and low recurrence and mortality rate, bad prognosis deduced from the negative ER and PR status despite the lack of HER-2/neu overexpression.

ACKNOWLEDGMENT

The author thanks to Yusuf Ibrahim for his assistance in dealing with the layout of the article.

REFERENCES

- Ama F (1990). Masalah kanker payudara dan pemecahannya. *Majalah Kesehatan Masyarakat Indonesia* 19
- Avis NE, Crawford S, Manuel J (2005). Quality of life among younger women with breast cancer. *J Clin Oncol* 23, 3322-3330
- Chang L (2009). Guide to Breast Cancer. Available from <http://www.webmd.com/breast-cancer/guide/breast-cancer-young-women>. Accessed May 18, 2011
- Ellis IO, Schnitt SJ, Sastre-Garau X, Bussolati G, Tavassoli FA, Eusebi V, Peterse JL, Mukai K, Tabar L, Jacquemier J, Cornelisse CJ, Sasco AJ, Kaaks R, Pisani P, Goldgar DE, Devilee P, Cleton-Jansen MJ, Borresen-Dale AL, van't Veer L, Sapino A (2003). Invasive breast carcinoma. In: Tavassoli FA and Devilee P (eds). *Pathology and Genetics of Tumours of the Breast and Female Genital Organs*, Lyon, IARC Press, p 13-41
- Fisher ER, Redmond CK, Liu H, Rockette H, Fisher B (1980). Correlation of estrogen receptor and pathologic characteristics of invasive breast cancer. *Cancer* 45, 349-353
- Kartika IEP, Maulani H, Sulastri H, Yuwono (2009). Ekspresi protein HER-2/neu, status reseptor estrogen dan progesteron pada berbagai derajat keganasan karsinoma payudara duktal invasif wanita usia muda. *Majalah Patologi* 18, 32-41
- Kumar V, Cotran RS, Robbins SL (2002). *Buku Ajar Patofisiologi* vol 1, 7th ed., New York, Elsevier Inc, p 193
- Ministry of Health, Republic of Indonesia (2008). Deteksi Singkat Dini Kanker Payudara, Jawaban untuk Menghindar. Available from <http://www.depkes.go.id/index.php>. Accessed June 24, 2011
- Payne SJ, Bowen RL, Jones JL, Wells CA (2008). Predictive markers in breast cancer--the present. *Histopathology* 52, 82-90
- Purnomosari D (2007). *Analisa Molekuler Penderita Kanker Payudara Usia Muda di Indonesia*. Yogyakarta, Universitas Gajah Mada Public Press
- Ross JS, Fletcher JA, Linette GP, Stec J, Clark E, Ayers M, Symmans WF, Pusztai L, Bloom KJ (2003). The Her-2/neu gene and protein in breast cancer 2003: biomarker and target of therapy. *Oncologist* 8, 307-325
- Sadhana U (2007). Kanker payudara wanita: ekspresi reseptor estrogen, reseptor progesteron dan HER-2. Available from <http://lib.atmajaya.ac.id/default.aspx?tabID=61&src=a&id=114594>. Accessed May 13, 2011.
- Tjindarbumi (1982). Penemuan dini kanker payudara dan penanggulangannya. In: *Diagnosis Dini Keganasan serta Penanggulangannya*, Jakarta, FKUI