

## HUBUNGAN ANTARA DERAJAT HISTOLOGI DAN STATUS LIMFONODI DENGAN SUBTIPE MOLEKULER KARSINOMA PAYUDARA DI RSUP DR. SARDJITO YOGYAKARTA

### INTISARI

**Latar Belakang.** Karsinoma payudara bersifat heterogen. Subtipe molekuler merupakan indikator prognosis dan terapi yang spesifik, demikian pula derajat histologi dan status limfonodi. Derajat histologi menunjukkan agresifitas sel tumor sedangkan status limfonodi berkaitan dengan risiko metastasis. Kajian mengenai hubungan derajat histologi maupun status limfonodi dengan subtipe molekuler karsinoma payudara di Indonesia berdasarkan lima penanda molekuler (ER, PR, HER2, Ki-67 dan CK5/6) masih terbatas.

**Tujuan.** Mengetahui profil subtipe molekuler pasien karsinoma payudara di RSUP Dr. Sardjito pada tahun 2012-2015 serta ada tidaknya hubungan antara derajat histologi dan status limfonodi dengan subtipe molekuler.

**Metode.** Subyek penelitian adalah blok parafin pasien karsinoma payudara invasif tahun 2012-2015. Berdasarkan kriteria eksklusi dan inklusi, didapatkan sampel sebanyak 248. Subtipe molekuler ditentukan menggunakan imunohistokimia ER, PR, HER2, Ki-67 dan CK5/6. Subtipe molekuler dibagi menjadi Luminal A (ER<sup>+</sup>/PR<sup>+</sup>/HER2<sup>-</sup>/Ki-67 <14%); Luminal B (ER<sup>+</sup>/PR<sup>+</sup>/HER2<sup>+</sup>/Ki-67 ≥14%); HER2-positif (ER<sup>-</sup>/PR<sup>-</sup>/HER2<sup>+</sup>) dan *triple negative breast cancers*/TNBC (ER<sup>-</sup>/PR<sup>-</sup>/HER2<sup>-</sup>). *Basal-like* merupakan TNBC dengan CK5/6<sup>+</sup>.

**Hasil.** Distribusi frekuensi menunjukkan bahwa Luminal A mempunyai frekuensi tertinggi sebesar 41,1%, kemudian TNBC (25,4%), HER2-*positive* (19,8%) dan Luminal B (13,7%). Hasil imunohistokimia CK5/6 pada 63 kasus TNBC menunjukkan bahwa 37 kasus (58,7%) merupakan *basal-like*. Derajat histologi berhubungan dengan subtipe ( $p=0,013$ ). Derajat histologi I didominasi oleh Luminal A sedangkan derajat histologi III didominasi oleh Luminal B, TNBC dan HER2-*positive*. Status limfonodi antar subtipe tidak menunjukkan perbedaan yang signifikan ( $p=0,547$ ).

**Kesimpulan.** Subtipe molekuler karsinoma payudara di Yogyakarta yang terbanyak adalah Luminal A, kemudian TNBC, HER2-*positive* dan Luminal B. Frekuensi *basal-like* lebih tinggi daripada *non basal-like*. Subtipe molekuler berhubungan dengan derajat histologi, namun tidak berhubungan dengan status limfonodi.

**Kata Kunci.** Karsinoma payudara, subtipe molekuler karsinoma payudara, derajat histologi, status limfonodi.

## ASSOCIATION BETWEEN HISTOLOGICAL GRADE AND LYMPH NODE METASTASES WITH MOLECULAR SUBTYPES OF BREAST CARCINOMA IN RSUP DR.SARDJITO YOGYAKARTA

### ABSTRACT

**Background:** Breast carcinoma is a heterogeneous disease and rich in diversity. Based on hormonal receptor expression (ER, PR, HER2) and molecular marker (Ki-67 and CK5/6), it can be categorized into Luminal A, Luminal B, HER2-positive and Triple Negative Breast Cancer (TNBC)/basal-like. Molecular subtypes of breast cancer is a strong prognostic and predictive factor. Besides, histological grade and lymph node metastases are independent prognostic factors. The study of breast cancer in Indonesia using five molecular biomarkers remains limited. Only few reports that have investigated the correlation between molecular subtypes with histological grade and lymph node metastasis.

**Methods:** We analyzed 248 invasive breast carcinoma cases from Department of Anatomic Pathology RSUP Dr. Sardjito between 2012-2015. The slides were stained for estrogen receptor (ER), progesterone receptor (PR), HER2, Ki-67 and CK5/6 for classification into breast cancer subtypes (BCS). Histological grade and lymph node status data were obtained from anatomic pathology records. The association between histological grade and lymph node status with BCS were examined.

**Results:** The immunohistochemical features of 250 cases of women with invasive breast carcinoma were examined. There were 102 patients with Luminal A (41,1%), 34 patients with Luminal B (13,7%), 49 patients with HER2-positive (19,8%), and 63 patients with TNBC (25,4%). Among 63 TNBC cases, 37 patients (58,7%) were positive for CK5/6 staining (basal-like). Statistically, there were significant differences between histological grade and subtypes ( $p=0,013$ ). However, significant differences were not found for lymph node metastasis ( $p=0,547$ ).

**Conclusions:** Luminal A has the highest proportions among TNBC, HER2-positive and Luminal B. Histological grade was associated with molecular subtypes of breast carcinoma in Yogyakarta, while lymph node metastasis was not. Grade I was associated with Luminal A, while Grade III was associated with Luminal B, HER2-positive and TNBC.

**Key words.** Breast carcinoma, molecular subtypes, histological grade, lymph node metastases.