INTISARI

Kanker payudara merupakan kanker utama di seluruh dunia dan terus meningkat terutama di negara berkembang dimana sebagian besar kasus ditemukan dalam stadium lanjut. Autofagi secara umum diaktifkan oleh kondisi kekurangan nutrisi, telah dihubungkan dengan fisiologi dan proses patologi seperti kanker. Protein terkait autofagi beclin 1 dan mTOR telah diketahui sebagai regulator insiasi autofagi. Beclin 1, regulator kunci autofagi, telah diketahui mengalami perubahan ekspresi pada berbagai kanker. *Mammalian target of rapamycin* (mTOR) kinase berfungsi mengintegrasi keadaan nutrisi dan faktor pertumbuhan. *The mammalian target of rapamycin* (mTOR) adalah regulator utama pertumbuhan sel dan proliferasi. mTOR kinase adalah regulator penentu induksi autofagi.

Tujuan penelitian adalah mengetahui inisiasi autofagi pada kanker payudara operabel. Evaluasi dilakukan dengan mengukur ekspresi protein beclin 1 dan mTOR pada tumor dengan pengecatan imunohistokimia.

Rancangan penelitian adalah *kohort retrospektif*. Subyek penelitian adalah penderita kanker payudara operabel. Pembedahan dilakukan pada 2010. Data klinikopatologi subyek dikumpulkan. Data ini meliputi usia, ukuran tumor, kelenjar getah bening, stadium, derajat diferensiasi histopatologi, ekspresi reseptor hormon, overekspresi reseptor HER2neu dan subtipe molekuler. Riwayat perkembangan penyakit terkait kanker payudara dilakukan evaluasi di tahun 2017, meliputi kekambuhan lokoregional, metastasis dan ketahanan hidup. Blok paraffin dikumpulkan. Dilakukan pemeriksaan dengan pengecatan imunohistokimia. Pemeriksaan dengan imunohistokimia dipergunakan untuk mendeteksi ekspresi protein beclin 1 dan mTOR pada tumor.

Tingkat ekspresi dari imunohistokimia dievaluasi secara visual dan analisis gambar dengan QUpath. Tingkat ekspresi dikategorikan lemah dan kuat dengan batas 50%. Hasil pemeriksaan dilakukan analisa hubungan dengan status klinikopatologi. Hasil dilakukan analisa dengan

analisis Kaplan Meier untuk mengetahui hubungannya dengan kekambuhan lokoregional, metastasis dan ketahanan hidup.

Terdapat 143 subyek, 75 subyek diperiksa imunohistokimia. Dari jumlah itu 60 dilakukan analisis gambar. Beberapa subyek tidak berhasil ditemukan. Beberapa data tidak lengkap. Setelah evaluasi keadaan operabilitas, 39 subyek dimasukkan ke dalam analisa statistik.

Hasil penelitian menunjukkan tidak ada hubungan yang bermakna antara ekspresi protein beclin 1 dengan usia, ukuran tumor, kelenjar getah bening, stadium, ekspresi hormonal reseptor estrogen dan progesteron, overekspresi HER2neu, dan subtipe molekuler. Tidak ditemukan hubungan yang bermakna antara eskpresi protein beclin 1dengan kekambuhan lokoregional, metastasis dan ketahanan hidup.

Hasil penelitian menunjukkan tidak ada hubungan antara ekspresi protein beclin 1 dan mTOR pada kanker payudara operabel dengan status klinikopatologi, kekambuhan lokoregional, metastasis dan ketahanan hidup.

Keywords : breast cancer, autophagy related protein, beclin 1, mTOR, immuohistochemistry, image analysis, clinicopathological status, locoregional recurrence, metastasis, survival, molecular subtype

ABSTRACT

Breast cancer is the top cancer in women worldwide and is increasing particularly in developing countries where the majority of cases are diagnosed in late stages. Autophagy is generally activated by conditions of nutrient deprivation but has also been associated with physiological as well as pathological processes such as cancer. The autophagy related protein beclin 1 and mTOR is known as autophagy initiation regulator. Beclin 1, a key regulator of autophagy, has been found to be aberrantly expressed in a variety of human malignancies. The mammalian target of rapamycin (mTOR) kinase integrates cues from nutrients and growth factors. The mammalian target of rapamycin (mTOR) is a master regulator of cell growth and proliferation. The kinase mTOR is a critical regulator of autophagy induction.

The aim of study is to evaluate the initiation of autophagy in the operable breast cancer. The evaluation was done by measuring the beclin 1 and mTOR protein expression in the tumor by immunohistochemical staining

The design is retrospective cohort. The subject were operable breast cancer. The surgery was done in 2010. The clinicopathological data of the subject were collected. The data include, age, tumor size, lymph node involvement, stage, grade, hormonal receptor expression, overexpression of HER2neu receptor and the molecular subtype. The history of breast cancer related condition were collected in 2017. The data include locoregional recurrence, metastasis and survival. The paraffin blocks were collected. The tissue were evaluated for immunohistochemical staining. Immunohistochemistry (IHC) were used to detect the protein expression of beclin 1 and mTOR in tumors.

The expression level of IHC were evaluated by visual examination and image analysis (QUpath). The level of expression categorized into weak and strong expression based on 50% cut off. The result were analyzed to evaluate its correlation with clinicopathological status. The result were

analyzed by Kaplan Meier survival analysis to evaluate its correlation to locoregional recurrence, distant metastasis and survival.

There were 143 subjects.75 were elligible for IHC. 60 slides were elligible for the image analysis. Some subjects can not be retraced. After reevaluation of the operable status and the data availability, 39 subject were included to the statistical analysis.

The result showed there is no significant correlation between beclin 1 protein expression and patient age, tumor size, lymph node involvement, pathological stage, hormonal estrogen and progesteron expression, HER2 neu overexpression, the molecular subtype . There is no significant correlation between beclin 1 protein expression and locoregional recurrence, distant metastasis and survival.

The result showed there is no significant correlation between mTOR protein expression and patient age, tumor size, lymph node involvement, pathological stadium, hormonal estrogen and progesteron expression, HER2neu overexpression, the molecular subtype . There is no significant correlation between mTOR protein expression and locoregional recurrence, distant metastasis and survival.

The study showed that there is no correlation between beclin 1 and mTOR expression from the operable breast cancer to clinicopathological status, locoregional recurrence, distant metastasis and survival.

Keywords : breast cancer, autophagy related protein, beclin 1, mTOR, immuohistochemistry, image analysis, clinicopathological status, locoregional recurrence, metastasis, survival, molecular subtype