ABSTRAK

Hubungan antara Ekspresi AEG-1 dan MMP-9
pada *Triple Negative Breast Cancer Operable*
dengan *Disease Free Survival.*

Latar belakang: Kanker payudara menempati peringkat pertama sebagai jenis kanker yang terdiagnosis di Indonesia. Kanker payudara *triple negative* atau *triple negative breast cancer* (TNBC) memiliki perilaku biologi sangat invasif, gradasi dan indeks mitosis yang tinggi, agresif serta prognosis yang buruk. *Astrocyte elevated gene-1* (AEG-1) adalah onkogen yang berperan penting pada proliferasi dan angiogenesis TNBC. MMP-9 berperan sebagai parameter invasi yang memainkan peran penting dalam remodeling matriks ekstraseluler dengan mendegradasi matriks ekstraseluler, yang meningkatkan pertumbuhan tumor payudara, invasi, metastasis, angiogenesis, dan proliferasi. Oleh karena itu AEG-1 dan MMP-9 berpotensi dapat digunakan sebagai penentuan prognosis pada TNBC *operable.*

Tujuan: Mengetahui hubungan dan ekspresi AEG-1 dan MMP-9 pada *Triple Negatif Breast Cancer Operable* dengan *Disease Free Survival*.

Metodologi penelitian: Penelitian ini merupakan penelitian *non-experimental analytic* dengan pendekatan metodologi *cohort*. Ekspresi AEG-1 pada spesimen jaringan tumor diperiksa secara qRT-PCR dengan menggunakan *Bioline SeniFast SYBR* dan SBS *Sangon Biotech Co Ltd,* Shanghai, China. Ekspresi MMP-9 pada spesimen jaringan tumor diperiksa secara qRT-PCR dengan menggunakan NucleoSpin RNA XS kit (Takara). RT-PCR dilakukan menggunakan BluePrint RT-PCR Kit (Takara) dalam thermal cycler. *Disease free survival* adalah periode waktu dimana tidak ditemukan lesi baru setelah operasi dilakukan yang dievaluasi dengan pemeriksaan penunjang pada lokoregional maupun metastasis jauh.

Hasil: Sampel penelitian sejumlah 54 pasien TNBC *Operable*. *Median survival* pasien dengan ekspresi AEG-1 tinggi adalah 9 bulan dan seluruh pasien adalah 31 bulan, ekspresi MMP-9 tinggi adalah 12 bulan dan seluruh pasien adalah 31 bulan. Terdapat hubungan yang signifikan antara ekspresi AEG-1 dengan DFS (p=0,000), antara MMP-9 dengan DFS (p=0,011). Ekspresi AEG-1 merupakan variabel paling berpengaruh terhadap DFS pada *Cox Regression* multivariat (p = 0,001 dan HR 5,363).

Kesimpulan: Terdapat hubungan yang signifikan antara AEG-1 dengan DFS dan MMP-9, MMP-9 dengan DFS.

Kata kunci: *Astrocyte Elevated Gene-1* (AEG-1), MMP-9, *Triple Negative Breast Cancer* (TNBC) *Operable*, *Disease Free Survival.*

Abstract

RELATIONSHIP BETWEEN AEG-1 AND MMP-9 EXPRESSION IN *OPERABLE TRIPLE NEGATIVE BREAST CANCER* WITH *DISEASE FREE SURVIVAL*

Fernando Silalahi*, Kunta Setiaji*, Paranita Ferronika **, Teguh Aryandono*
*Department of Surgery, Surgical Oncology Division, Faculty of Medicine, Public Health, andNursing, Gadjah Mada University/ dr. Sardjito Hospital, Yogyakarta
** Department of Anatomical Pathology, Faculty of Medicine, Public Health, and Nursing, Gadjah Mada University/ dr. Sardjito Hospital, Yogyakarta

Background: Breast cancer ranks first as a type of cancer diagnosed in Indonesia. Triple negative breast cancer (TNBC) has a highly invasive biological behavior, high mitotic grade and index, aggressive and poor prognosis. Astrocyte elevated gene-1 (AEG-1) is an oncogene that plays an important role in the proliferation and angiogenesis of TNBC. MMP-9 acts as an invasion parameter that plays an important role in extracellular matrix remodeling by degrading the extracellular matrix, which increases breast tumor growth, invasion, metastasis, angiogenesis, and proliferation. Therefore, AEG-1 and MMP-9 have the potential to be used as prognostic determinants in operable TNBC.

Purpose: Analyzing the relationship between AEG-1 expression and DFS, the relationship between MMP-9 expression and DFS, and the relationship between AEG-1 and MMP-9 expression in Operable Triple Negative Breast Cancer

Subjects and Methods: This cohort study involved 54 samples of TNBC Operable breast cancer patients. qRT-PCR examination was performed to assess AEG-1 expression and then categorized into low and high expression based on the optimal cut off. Univariate and multivariate analysis in this study used the Cox regression test to see which independent variables were more closely related to the dependent variable. Bivariate analysis used the Chi-Square test. The Kaplan-Meier and log-rank methods were used to assess survival analysis.

Results: The study sample consisted of 54 Operable TNBC patients. The median survival of patients with high AEG-1 expression was 9 months and all patients were 31 months, high MMP-9 expression was 12 months and all patients were 31 months. There was a significant relationship between AEG-1 expression and DFS ($p = 0.000$), between MMP-9 and DFS ($p = 0.011$). AEG-1 expression was the most influential variable on DFS in multivariate Cox Regression ($p = 0.001$ and HR 5.363).

Conclusion: There was a significant association between AEG-1 and MMP-9, AEG-1 and DFS, MMP-9 and DFS.

Keywords: AEG-1, MMP-9,TNBC, DFS