

Abstrak

Ekspresi miR-193b, miR-222 Plasma pada Metastasis Kanker Payudara. Studi Hubungan terhadap *Urokinase Plasminogen Activator*

Sheella Bororing, Budi Mulyono, Sofia Mubarika, Teguh Aryandono

Kanker payudara merupakan penyebab tersering kematian akibat kanker pada kaum perempuan. Sebagian besar kematian akibat metastasis. Proses awal metastasis ditandai oleh degradasi matriks ekstraseluler dan *epithelial mesenchymal transition* (EMT). Proses degradasi matriks ekstraseluler diperankan oleh uPA dan inhibitornya (PAI-1), sedangkan E-Cadherin dan N-Cadherin merupakan penanda proses EMT. Tujuan penelitian ini adalah mengetahui kemampuan ekspresi miR-193b, miR-222 di plasma terhadap ekspresi uPA jaringan yang diketahui mempunyai nilai prognosis pada kanker payudara. Diamati juga peran miR-222 terhadap E-Cadherin dan N-Cadherin.

Penelitian ini adalah penelitian observasional analitik dengan rancangan potong lintang terhadap 45 orang wanita penderita kanker payudara primer dan yang metastasis ke kelenjar getah bening. Ekspresi mRNA uPA, PAI-1, E-Cadherin, N-Cadherin diperiksa dari sediaan *Formalin Fixed Paraffin Embedded* (FFPE), sedangkan ekspresi miR-193b, miR-222 dari plasmanya. Pemeriksaan sampel menggunakan qRT-PCR, yang hasilnya diperoleh dengan metode kuantifikasi relatif.

Total subyek penelitian yang mengikuti penelitian ini adalah sebanyak 55 orang. Rerata usia $48,42 \pm 9,42$ (24 sampai 71 tahun). Sebagian besar pasien menderita tumor ganas payudara tipe *Invasive Ductal Carcinoma* (IDC), grade III, yang berukuran lebih dari 2 cm, sudah bermetastasis ke kelenjar getah bening, dengan subtype luminal. Tidak didapatkan hubungan dan korelasi yang bermakna antara uPA, PAI-1, E Cadherin, N Cadherin, miR-193b, miR-222 dengan metastasis ke kelenjar getah bening. Korelasi miR-193b plasma dengan uPA ($r = -0,09$, $p = 0,55$), korelasi antara miR-222 terhadap uPA ($r = -0,10$, $p = 0,49$), korelasi miR-222 terhadap E-Cadherin ($r = 0,09$, $p = 0,55$), korelasi miR-222 terhadap N-Cadherin ($r = -0,26$, $p = 0,07$). Hasil analisis jalur ini menunjukkan hubungan langsung antara miR-193b dan miR-222 terhadap metastasis kelenjar getah bening lebih kuat dibandingkan melalui uPA sebagai mediator. Berdasarkan analisis multivariat, didapatkan persamaan regresi dengan model $= 1,13 - 2,26 \text{ miR-193b} + 7,03 \text{ miR-222} + 0,29 \text{ uPA}$.

Kata kunci: miR-193b, miR-222, *urokinase Plasminogen Activator*, kanker payudara, metastasis.

Abstract

*The Expression of plasma miR-193b,miR-222 on the breast cancer metastasis.
The association study to urokinase Plasminogen Activator*

Sheella Bororing, Budi Mulyono, Sofia Mubarika, Teguh Aryandono

Breast cancer is the most common cause of cancer deaths among women. Most of the deaths is caused by metastasis. The initial process of metastasis consist of by degradation of extracellular matrix and epithelial mesenchymal transition (EMT). The extracellular matrix degradation process is roled by uPA and its inhibitor (PAI-1), while E-Cadherin and N-Cadherin are markers of the EMT process. The objectives of this study are to determine the ability of miR-193b, miR-222 in plasma against tissue uPA. uPA have a prognostic value in breast cancer. This study also analyze the of miR-222 against E-Cadherin and N-Cadherin.

This was an observational analytic study with cross sectional design on 45 women with breast cancer with or without metastases to lymph nodes. We examined mRNA uPA, PAI-1, E-Cadherin, N-Cadherin from FFPE, whereas miR-193b, miR-222 from plasma. We used qRT-PCR methods and the results obtained by relative quantification method.

The total subjects who participated in this study were 55 people. The mean age was 48.42 ± 9.42 (24 to 71 years). Most patients are Invasive Ductal Carsinoma (IDC) type, grade III, which are more than 2 cm in size, have metastasized to lymph nodes, with luminal subtypes. There was no significant association and correlation between uPA, PAI-1, E-Cadherin, N-Cadherin, miR-193b, miR-222 and lymph node metastasis. The Spearman test revealed no significant correlation between miR-193b and uPA ($r = -0.09$, $p = 0.55$); miR-222 and uPA ($r = -0.10$, $p = 0.49$); miR-222 and E-Cadherin ($r = 0.09$, $p = 0.55$); miR-222 and N-Cadherin ($r = -0.26$, $p = 0.07$). The results of pathway analysis showed that direct association between miR-193b and miR-222 to lymph node metastasis was stronger than the indirect (mediated by uPA). Based on the multivariate analysis, the regression of equation model= $1.13 - 2.26 \text{ miR-193b} + 7.03 \text{ miR-222} + 0.29 \text{ uPA}$.

Keywords: miR-193b, miR-222, urokinase Plasminogen Activator, breast cancer, metastasis