

ABSTRACT

**Association Between Plasma Urokinase Plasminogen Activator (uPA) Expression and
Clinicopathological Factors with Disease-Free Survival in Non-Metastatic Breast Cancer
Patients**

Mochamad Reza Febrian", Sumadi Lukman * , Teguh Aryandono Dewi Kartikawati Paramita "

* Department of Surgery, Faculty of Medicine, Public Health, and Nursing (Universitas Gadjah Mada / Dr. Sardito General Hospital, Yogyakarta, Indonesia ** Department of Anatomical Pathology, Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada/ Dr. Sardito General Hospital, Yogyakarta, Indonesia

Background: Breast cancer ranks first among the most frequently diagnosed cancers in Indonesian women. Suboptimal and uneven early-detection programs result in many patients being diagnosed at advanced stages. Urokinase plasminogen activator (uPA) is a serine protease involved in extracellular matrix remodeling and cell migration—two key processes associated with tumor progression and metastasis. Elevated uPA levels in tumor tissue and plasma have demonstrated strong prognostic value. With a more affordable cost compared to PCR-based assays, plasma uPA measurement can be a feasible option in various healthcare settings.

Objective: To evaluate the association between plasma urokinase plasminogen activator (uPA) levels and disease-free survival (DFS) in patients with non-metastatic breast cancer.

Methods: This study employed a non-experimental analytical design using a retrospective cohort approach. Plasma uPA levels were measured using ELISA (Reed Biotech Co. Ltd.). Data on disease-free survival were obtained from the medical records of Dr. Sardjito General Hospital. Disease-free survival was defined as the time interval during which no new lesions were detected following surgery, assessed through imaging and clinical evaluation for locoregional recurrence or distant metastasis.

Results: A total of 87 non-metastatic breast cancer patients were included. The mean disease-free survival among patients with low uPA levels was 20.14 months, whereas those with high uPA levels had a mean DFS of 11.16 months, with a median DFS of 8 months. Overall, the average DFS for both groups was 16.94 months. The Log-Rank test showed $\chi^2 = 30.08$ with $p = 0.000$. Plasma uPA level was the most influential variable in multivariate Cox regression analysis. Patients with high uPA levels (≥ 0.8550 pg/ μ L) had a 3.84-fold higher risk of recurrence compared to those with low levels ($p = 0.00$; HR = 3.842).

Conclusion: High plasma uPA levels are significantly associated with poorer disease-free survival in non-metastatic breast cancer patients.

Keywords: uPA (urokinase plasminogen activator), clinicopathological factors, breast cancer, early breast cancer, locally advanced breast cancer, disease-free survival.

Hubungan Ekspresi *Urokinase Plasminogen Activator* (uPA) Plasma Darah Dan Klinikopatologi
Disease Free Survival Pasien Kanker Payudara Non Metastase

Latar belakang: Kanker payudara menempati peringkat pertama sebagai jenis kanker pada wanita yang terdiagnosis di Indonesia. Program deteksi dini yang tidak optimal dan tidak merata menyebabkan sebagian besar pasien terdiagnosis pada stadium lanjut. *Urokinase plasminogen activator* (uPA) adalah protease serin yang terlibat dalam remodeling matriks ekstraseluler dan migrasi sel, dua peristiwa yang sangat berhubungan dengan perkembangan dan penyebaran kanker. Kadar uPA meningkat di jaringan tumor dan plasma darah pada penderita kanker dapat menjadi alat prognosis yang kuat. Dengan harga yang lebih terjangkau dari pemeriksaan PCR menjadi pemeriksaan yang bisa di aplikasikan di daerah.

Tujuan: Mengetahui hubungan kadar uPA (*urokinase plasminogen activator*) pada plasma darah dengan *disease free survival* pasien kanker payudara non metastase.

Metodologi : Penelitian ini merupakan penelitian *non-experimental analytic* dengan pendekatan metodologi *retrospective cohort*. Kadar urokinase plasminogen activator pada plasma darah pasien tumor diperiksa secara ELISA dengan menggunakan *Reed Biotech Co Ltd*. Data *disease free survival* didapatkan dari catatan rekam medis RSUP Dr. Sardjito. *Disease free survival* adalah periode waktu dimana tidak ditemukan lesi baru setelah operasi dilakukan yang di evaluasi dengan pemeriksaan penunjang pada lokoregional maupun metastasis jauh.

Hasil : Sampel penelitian sejumlah 87 pasien kanker payudara non metastase. menunjukkan rata-rata waktu *Disease Free Survival* pada kelompok kadar *urokinase Plasminogen Activator* (uPA) rendah adalah 20,14 bulan, sedangkan pada kelompok kadar uPA tinggi sebesar 11,16 bulan dengan median DFS sebesar 8 bulan. Secara keseluruhan, rata-rata DFS responden dengan kadar uPA rendah dan tinggi adalah 16,94 bulan. Hasil uji *Log Rank* menunjukkan nilai $\chi^2 = 30,08$ dan $p \text{ value} = 0,000$. Kadar uPA merupakan variabel paling berpengaruh terhadap DFS pada Cox Regression multivariat Pasien dengan kadar uPA tinggi ($\geq 0,8550 \text{ pg}/\mu\text{L}$) memiliki risiko kekambuhan sebesar 3,84 kali lebih tinggi dibandingkan dengan kadar uPA rendah ($p=0,00$ dan $HR = 3,842$)

Kesimpulan : Terdapat hubungan yang signifikan antara kadar uPA darah yang tinggi dengan DFS

Kata kunci: UPA (*urokinase plasminogen activator*), klinikopatologi, breast cancer , early breast cancer, locally advance breast cancer , *disease free survival*.