

Nilai Prognostik Neutropenia Pasca Kemoterapi Awitan Dini Terhadap Kesintasan Pasien Kanker Payudara *Triple Negative* di RSUP Dr Sardjito

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Intisari

Latar Belakang: Kanker payudara adalah kanker yang paling banyak ditemukan pada wanita di dunia, termasuk di Indonesia dan RSUP Dr Sardjito. Subtipe kanker payudara yang paling umum ditemui di Indonesia adalah luminal A, diikuti subtipe *triple – negative*. Kanker payudara *triple – negative* atau *triple negative breast cancer* (TNBC) adalah jenis kanker payudara yang menunjukkan gambaran histopatologis negatif pada reseptor hormonal dan HER2, sehingga pilihan perawatan TNBC masih terbatas pada pembedahan, radioterapi, dan kemoterapi. Kemoterapi, sebagai opsi yang paling disarankan, menekan sistem hematopoietik dan mekanisme imunitas pasien sehingga dikaitkan dengan terjadinya neutropenia. Neutropenia yang diinduksi kemoterapi (*chemotherapy-induced neutropenia* / CIN) adalah toksisitas hematologi yang paling serius dari kemoterapi kanker. Berdasarkan waktu terjadinya, CIN dibagi menjadi awitan dini dan awitan akhir, yang diperkirakan dapat menjadi faktor prognostik terhadap kesintasan pasien kanker.

Tujuan: Mengetahui pengaruh kondisi neutropenia pasca kemoterapi awitan dini terhadap angka *overall survival* (OS) 2 tahun pada pasien TNBC di RSUP Dr Sardjito.

Metode: Penelitian ini menggunakan metode studi observasional analitik, dengan desain kohort retrospektif. Sumber data adalah registri klinis pasien TNBC di Instalasi Kanker Tulip RSUP Dr. Sardjito Yogyakarta tahun 2014-2018. Penelitian ini menggunakan analisis kesintasan yang berupa *overall survival* (OS) dengan indikator CIN yang dijadikan sebagai variabel bebas yang selanjutnya akan diuji pengaruhnya terhadap kesintasan pasien (variabel terikat). Subjek penelitian didapat melalui teknik *sampling* konsekutif. Kesintasan dianalisis menggunakan kurva *Kaplan-Meier* dan dibandingkan dengan uji log-rank, diikuti dengan analisis univariat pada model *cox-proportional hazard*.

Hasil: Neutropenia awitan dini yang diinduksi kemoterapi terdapat pada 42 pasien (43,3%) dari total 97 pasien penelitian. Pasien yang meninggal berjumlah 37 (21 pada kelompok neutropenia dan 16 pada kelompok non-neutropenia), dan pasien yang hidup pada akhir penelitian berjumlah 60 (34 pada neutropenia dan 26 pada non-neutropenia) ($P=0,993$) yang mengindikasikan hubungan tidak signifikan antara neutropenia dan luaran. Pada uji Log-rank didapatkan bahwa hasil *2-year survival* CIN sebesar 60,2% dengan rata-rata waktu kesintasan $41,079 \pm 3,42$ bulan dan median waktu kesintasan 46 bulan ($p=0,488$). Analisis kesintasan dengan model *cox-regression* menunjukkan bahwa neutropenia memengaruhi OS, namun tidak bermakna secara statistik (HR 0,794; IK 95%: 0,414 – 1,524; $P= 0,489$). Dari hasil analisis univariat beberapa parameter diantaranya usia, indeks massa tubuh, stadium klinis, tipe histologi, tipe operasi, regimen kemoterapi, dan anemia pre-kemoterapi, hanya status anemia pre-kemoterapi yang memiliki pengaruh signifikan ($P= 0,037$).

Kesimpulan: Neutropenia pasca kemoterapi awitan dini bukan merupakan faktor prognostik independen terhadap luaran pasien TNBC di Instalasi Kanker Tulip, RSUP Dr Sardjito.

Kata Kunci: Neutropenia, *triple negative breast cancer*, kesintasan.

Prognostic Value of Early Onset Chemotherapy-Induced Neutropenia to Triple Negative Breast Cancer Patients Survival at Dr Sardjito Hospital

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Abstract

Background: Breast cancer is the most common cancer among women worldwide, including in Indonesia and Dr. Sardjito Hospital. The most common breast cancer subtype found in Indonesia is Luminal A, followed by the triple - negative subtype. Triple negative breast cancer (TNBC) is a type of breast cancer that shows negative histopathological features at hormonal receptors and HER2, making treatment options for TNBC to be limited to surgery, radiotherapy and chemotherapy. Chemotherapy, as the most preferred option, suppresses the hematopoietic system and the patient's immune mechanisms, and is therefore associated with neutropenia. Chemotherapy-induced neutropenia (CIN) is the most serious hematologic toxicity of cancer chemotherapy. Based on the time of occurrence, CIN is divided into early onset and late onset, which is thought to be a prognostic factor for the survival of cancer patients.

Objective: Identifying the impact of chemotherapy-induced neutropenia towards the 2-year overall survival (OS) rate in TNBC patients at Dr. Sardjito General Hospital.

Method: This research used an analytic observational method, with a retrospective cohort design, using data that was obtained from the clinical registry of TNBC patients at the Tulip Cancer Center, Dr. Sardjito Hospital Yogyakarta from 2014-2018. This study used a survival analysis in the form of overall survival (OS) with early-onset CIN as the independent variable, which will then be tested for its relation to the patients' survival (dependent variable). The sampling technique used was consecutive sampling. Patient's survival was analyzed using the Kaplan-Meier curve and compared with the log-rank test, followed by univariate analysis on a cox-proportional hazard model.

Results: Early onset chemotherapy-induced neutropenia was present in 42 patients (43.3%) out of the total 97 study patients. There were 37 patients who died (21 in the neutropenic group and 16 in the non-neutropenic group), and 60 patients alive at the end of the study (34 in neutropenia and 26 in non-neutropenia) ($P = 0.993$) indicating an insignificant relationship between neutropenia and output. In the Log-rank test, it was found that the 2-year survival result was 60.2% with mean survival time $41,079 \pm 3,42$ months and median survival time 46 months ($p = 0.488$). The survival analysis using the cox-regression model showed that CIN affected OS (HR 0,794; 95% CI: 0.414 - 1.524; $P = 0.489$), but it was not statistically significant. From the results of the univariate analysis of several parameters including age, body mass index, clinical stage, histological type, type of surgery, chemotherapy regimen, and pre-chemotherapy anemia, only pre-chemotherapy anemia status had a significant effect ($P = 0.037$).

Conclusion: Early onset chemotherapy-induced neutropenia is not an independent prognostic factor for the outcome of TNBC patients at the Tulip Cancer Installation, Dr. Sardjito Hospital.

Keywords: Neutropenia, early onset chemotherapy-induced neutropenia, triple negative breast cancer, survival rate