

HUBUNGAN ANTARA EKSPRESI p53 MUTAN DAN RESPON KEMOTERAPI NEOADJUVAN PADA KANKER SERVIKS STADIUM II

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ABSTRAK

LATAR BELAKANG: Kanker serviks masih merupakan masalah kesehatan perempuan di Indonesia dengan angka kejadian dan kematian yang tinggi. Pada kanker serviks stadium IB2, IIA2 dan IIB dikenalkan modalitas “*Protocol Buenos Aires*” sebagai kemoterapi neoadjuvan sebelum operasi radikal untuk mengurangi massa tumor sehingga memudahkan pembedahan dan menghambat mikrometastasis. Infeksi HPV sebagai faktor penting dalam patogenesis kanker serviks, dapat mengakibatkan gangguan pada p53. Sampai saat ini, belum ada prediktor yang digunakan untuk memprediksi respon kemoterapi neoadjuvan pada kanker serviks.

TUJUAN: Mengetahui hubungan antara ekspresi p53 mutan dan respon kemoterapi neoadjuvan pada kanker serviks stadium II.

MATERIAL DAN METODE: Penelitian ini adalah *kohort retrospektif* melibatkan 35 dari 82 pasien yang memenuhi kriteria kelayakan. Dari blok parafin jaringan serviks dilakukan pengecatan immunohistokimia dengan antibodi primer antimutan p53. Kelompok penelitian terdiri atas ekspresi p53 mutan positif dan negatif. Respon kemoterapi dinilai secara klinis dan kriteria RECIST. Variabel luar yang dievaluasi adalah stadium, histopatologi, derajat diferensiasi dan regimen kemoterapi. Analisis data dengan uji *Chi square* dan uji regresi logistik

HASIL: Dari 35 subyek, 77,14% tidak respon kemoterapi, 17,41% dengan positif ekspresi p53 mutan. Berdasarkan analisis bivariat, respon kemoterapi neoadjuvan tidak signifikan berbeda antara ekspresi p53 mutan positif vs negatif ($p=0,582$; RR 1,098; CI 95% 0,727 – 1,659). Hasil analisis multivariat mendapatkan bahwa kanker serviks stadium II dengan positif ekspresi p53 mutan ($p=0,423$; OR 3,121; CI 95% 0,193-50,601) dan derajat diferensiasi buruk mempunyai kemungkinan tidak respon terhadap kemoterapi neoadjuvan ($p=0,013$; OR 12,863; CI 95% 1,723-96,052).

KESIMPULAN: Pada kanker serviks stadium II, ekspresi p53 mutan positif tiga kali lebih besar berhubungan dengan tidak respon terhadap kemoterapi neoadjuvan dibandingkan dengan ekspresi p53 mutan negatif.

KATA KUNCI: ekspresi p53 mutan, kanker serviks stadium II, kemoterapi neoadjuvan, respon terapi.

THE CORRELATION BETWEEN MUTANT p53 EXPRESSION AND NEOADJUVANT CHEMOTHERAPY RESPONSE IN STAGE II CERVICAL CANCER

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Abstract

BACKGROUND: Cervical cancer is still one of women's health problem in Indonesia with high incidence and mortality rate. The introduced modality for Stage IB2, IIA2 and IIB cervical cancer is named as "Protocol Buenos Aires" used as neoadjuvant chemotherapy before radical operation to reduce tumor mass in order to simplify the operation procedure and to inhibit the micro-metastasis. HPV Infection as important factor in cervical cancer pathogenesis and could cause p53 disruption. Unfortunately, no available predictor used to predict the neoadjuvant chemotherapy response in cervical cancer.

OBJECTIVE: To find the association between p53 mutant expression and neoadjuvant chemotherapy response in stage II cervical cancer.

MATERIAL AND METHOD: This was cohort-retrospective study that involved 35 of 82 patients fulfilled to the eligible criteria. Primary antibody p53 anti-mutant was used for immunohistochemical staining in cervical tissue paraffin block. Study group consisted of positive p53 mutant expression and negative p53 mutant expression. Chemotherapy response was assessed clinically and based on RECIST criteria. The assessed external variable is stage, degree of differentiation, and chemotherapy regimen. Data was analysed using Chi square Test and logistic regression test.

RESULT: Of 35 subjects, 77.14% not responded to chemotherapy, 17.41% with positive p53 mutant expression. Based on bivariate analysis, neoadjuvant chemotherapy response was not significantly different between positive p53 mutant expression and negative p53 mutant expression ($p=0.582$; RR 1.098; CI 95% 0.727 – 1.659). The result of multivariate analysis results that stage IIA and IIB cervical cancer with positive p53 mutant expression ($p=0.423$; OR 3.121; CI 95% 0.193-50.601) and poor degree of differentiation had probability for not responded to neoadjuvant chemotherapy ($p=0.013$; OR 12.863; CI 95% 1.723-96.052).

CONCLUSION: Stage II cervical cancer, positive p53 mutant expression three times higher associated with non-response neoadjuvant chemotherapy compared to negative p53 mutant expression

KEYWORDS: p53 mutant expression, stage II cervical cancer, neoadjuvant chemotherapy, response therapy.