

# Kadar survivin, telomerase, dan sitokrom c sebagai prediktor respons terapi pada pasien karsinoma sel skuamosa serviks stadium iiib = Levels of survivin telomerase and cytochrome c as predictor of therapeutic response in patients with stage iiib squamous cell carcinoma of cervix

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## Abstrak

Angka kematian kanker serviks masih tinggi karena banyak pasien datang berobat pada tahap lanjut. Respons terapi radiasi pada pasien kanker serviks stadium lanjut bervariasi walau dengan faktor klinikopatologi yang sama seperti stadium, massa tumor, jenis histopatologi, derajat diferensiasi, invasi limfovaskular, reaksi limfosit dan nekrosis. Oleh karena itu dipikirkan faktor prognosis lain seperti faktor apoptosis-survivin, telomerase dan sitokrom c.

Penelitian ini bertujuan untuk mengetahui peran survivin, telomerase, dan sitokrom c sebagai prediktor respons terapi radiasi pada kanker serviks stadium lanjut khususnya stadium IIIB. Studi ini bersifat prospektif menggunakan metode nested case control. Pengambilan data dilakukan di Poliklinik Onkologi Departemen Obstetri dan Ginekologi RSCM serta Departemen Patologi Anatomi FKUI pada bulan Januari 2016 hingga Mei 2017. Pada subjek penelitian dilakukan wawancara, pemeriksaan histopatologi dan pemeriksaan biokimia secara ELISA untuk mengetahui kadar survivin, telomerase, sitokrom c, dan MRI pra-radiasi serta pasca-radiasi.

Dari 90 subjek penelitian didapatkan rerata usia pasien 50 tahun, rerata massa tumor 6,7 cm dan sebagian besar berkeratin 84,4, berdiferensiasi baik 81,1, reaksi limfosit negatif 75,6 dan nekrosis 74,4. Rerata faktor apoptosis-survivin, telomerase dan sitokrom c adalah 591,2 pg/mL, 5.223,2 pg/mL dan 191,3 ng/mL. Dari analisis bivariat didapatkan variabel yang berhubungan dengan respons terapi secara independen adalah massa tumor  $p = 0,1$ , diferensiasi  $p = 0,17$ , kadar survivin  $p = 0,01$ , kadar telomerase  $p = 0,08$  dan kadar sitokrom c  $p = 0,47$ .

Hasil analisis multivariat didapatkan hubungan kadar survivin dan kadar telomerase dengan respons terapi radiasi  $p = 0,01$  dan  $p = 0,07$ . Tidak terdapat hubungan kadar sitokrom c dengan respons terapi radiasi  $p = 0,64$ . Dengan model cox regresi survival didapatkan hazard ratio subjek dengan kadar survivin tinggi dan kadar telomerase tinggi terhadap respons terapi radiasi negatif adalah 4,20 dan 1,97. Simpulan: kadar survivin dan telomerase tinggi berhubungan dengan respons terapi radiasi negatif.

.....Cervical cancer mortality rate is still high mostly due to patients seeking for help in advanced stage of the disease. Even with the same clinicopathologic features such as stage of the diseases, size of the tumor, histopathological types, level of differentiation, lymphocyte reaction and tumor necrosis, the radiotherapy outcomes still vary from patient to patient. Therefore, we thought another predictive factors like apoptosis inducing factors i.e. survivin, telomerase and cytochrome c as a new predictor of therapeutic responses on patients with stage IIIB squamous cell carcinoma of cervix.

This is a prospective study with nested case control method. Data collection was conducted in Oncology Polyclinic, Department of Obstetrics and Gynecology RSCM and Department of Pathological Anatomy of FKUI from January 2016 to May 2017. Subjects were interviewed, conducted histopathological and biochemical examination with ELISA to determine levels of survivin, telomerase, cytochrome c, and

patients undergo pre and post radiation MR imaging.

There were 90 patients in this study with the mean of ages was 50 years, mean of tumor size was 6.7 cm and most subjects were keratinizing 84.4 , well differentiated 81.1 , negative lymphocyte reaction 75.6 and tumor necrosis 74.4 . The mean levels of apoptosis inducing factors survivin, telomerase and cytochrome c were 591.2 pg mL, 5,223.2 pg mL, and 191.3 ng mL.

Bivariate analysis showed the independent association between tumor size, level of differentiation, levels of survivin and telomerase p 0.1, p 0.17, p 0.01, p 0.08 . Multivariate analysis showed the correlation between levels of survivin and telomerase with radiation therapeutic response p 0.01 and p 0.07 and there was no association with level of cytochrome c p 0.64 With the survival cox regression models, the hazard ratio of subjects with high levels of survivin and telomerase on the negative radiation therapy responses were 4.20 and 1.97. Conclusion there were association between high levels of survivin and telomerase on the negative radiation therapy response.