

# Model prediksi status mutasi kras pada adenokarsinoma kolorektal tipe serrated berdasarkan gambaran histomorfologik serta ekspresi P53 dan BCL-2 = Prediction model of kras mutation status in colorectal serrated adenocarcinoma based on histomorphological features and expression of P53 and BCL 2

Diah Rini Handjari, author

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## Abstrak

### <b>ABSTRAK</b><br>

Kanker kolorektal KKR dianggap sebagai masalah kesehatan utama, salah satu jenis kanker yang paling sering terjadi serta penyebab kematian kedua terbesar di negara barat dan di Indonesia. Adenokarsinoma kolorektal serrated AKS merupakan salah satu tipe dari KKR. Salah satu jalur karsinogenesis kolorektal adalah jalur serrated yang diketahui melibatkan mutasi gen KRAS. Penanda tumor lain yang juga terlibat dalam proses karsinogenesis adalah P53 dan Bcl-2. Gambaran histomorfologik yang ditemukan oleh Tuppurainen dkk. saat ini digunakan sebagai penanda AKS. Terbatasnya sarana laboratorium patologi molekular di Indonesia, menekankan pentingnya membuat model skoring gambaran histomorfologik AKS dan atau ekspresi protein P53 serta Bcl-2 untuk memprediksi mutasi KRAS. Penelitian potong lintang terhadap 39 kasus AKS didapatkan dari Arsip Departemen Patologi Anatomi FKUI/RSCM selama tahun 2013 ndash;2015. Setiap kasus dikumpulkan data klinisnya, dan dinilai ulang karakteristik histomorfologik dan penanda tumor Bcl2 dan P53 , serta dilakukan pemeriksaan status KRAS. Penelitian histomorfologik dilakukan per kasus dan per contoh yaitu terhadap 100 kelenjar/kasus. Pada penelitian ini, kasus AKS ditemukan paling banyak pada laki-laki 51,3 , usia ge; 40 tahun 71,8 , lokasi di kolon kiri 84,6 , tidak memiliki metastasis 92,3 , status mutasi KRAS 71,8 . Ekspresi protein P53 didapatkan pada 69,2 dan protein Bcl-2 51,3 , tidak didapatkan hubungan bermakna ekspresi protein tersebut dengan status KRAS. Gambaran histomorfologik status KRAS didapatkan hubungan pada epitel serrated, lokasi inti sel, kondisi inti, sitoplasma dan musin. Odds ratio tertinggi ditemukan pada epitel serrated OR 2,7; IK 95 2,30 ndash;3,07 dan musin OR 2,0; IK 95 , 1,15 ndash;3,65 . Berdasarkan uji statistik didapatkan model nilai skoring yang terdiri dari epitel serrated, keadaan lokasi inti, kondisi inti dan adanya musin CI 95 antara 61 ndash;65 . Nilai sensitivitas dan spesifisitas berdasarkan nilai titik potong pada angka 16 sensitivitasnya sebesar 72 dan spesifisitasnya sebesar 48 . Simpulan: Didapatkan model sistem skor dengan titik potong 16 untuk memprediksi adanya mutasi KRAS berdasarkan, epitel serrated, lokasi inti sel, kondisi inti, dan adanya musin. Kata kunci: Adenokarsinoma kolorektal serrated, Bcl-2, jalur serrated, Kanker kolorektal, mutasi KRAS, P53

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### <b>ABSTRACT</b><br>

Colorectal cancer CRC is considered as major health problem, one type of cancer that most often occurs as well as the second largest cause of death in western countries and in Indonesia. Serrated colorectal adenocarcinoma SA is one type of CRC. One of colorectal carcinogenesis pathway is serrated pathway that known to involve KRAS gene mutation. Other tumor markers that also involved in the process of its carcinogenesis were P53 and Bcl 2. Histomorphological criteria found by Tuppurainen et al currently used

as marker of SA. Limited facilities of molecular pathology laboratory in Indonesia emphasize the needs of making scoring model by using histomorphological features of SA and or P53 and Bcl 2 protein expression to predict KRAS mutation. A cross sectional study conducted to 39 cases of SA registered in Departement of Anatomical Pathology FMUI Ciptomangunkusumo Hospital from 2013 ndash 2015. All clinical data related to the cases were collected. Each case was reevaluated based on Tuppurainen histomorphological criteria, tumor markers Bcl 2 and P53 , and KRAS status. Histomorphological examination is conducted per case and per instance to 100 nodes case. Present study showed that most cases of SA was found in male 51.3 , aged ge 40 years 71.8 , located in left colon 84.6 , did not have metastasis 92.3 , with KRAS mutation status 71.8 . P53 and Bcl 2 protein expressions were found in 69.2 and 51.3 respectively, with no significant association with KRAS status. Histomorphological features of KRAS status found in epithelial serration, nucleus location, nucleus condition, cytoplasm and mucin. Epithelial serration has the highest odds ratio OR 2.7 IK 95 2.30 ndash 3.07 followed by mucin OR 2.0 IK 95 , 1.15 ndash 3.65 . Statistical values showed scoring models consisted of epithelial serrations, nucleus location, nucleus condition and presence of mucin CI 95 between 61 ndash 65 . The sensitivity and specificity cut off point located on the number 16, with sensitivity value was 72 and specificity 48 . Conclusion A scoring system model yielded 16 as cut off score was obtained to predict KRAS mutations based on epithelial serrations, nucleus location, nucleus condition and presence of mucin. Keywords Bcl2, Colorectal cancer, colorectal serrated adenocarcinoma, KRAS mutation, P53, serrated pathway