Profil Mutasi Patogenik Gen APC, KRAS, TP53, PIK3CA, dan MLH1 pada Adenokarsinoma Kolorektal berdasarkan Perangai dan Kesintasan = Indonesian Genomic Landscape of Pathogenic Mutation of APC, KRAS, TP53, PIK3CA, and MLH1 in Colorectal Cancer

Vania Myralda Giamour, author

Abstrak

Latar Belakang : Keganasan kolorektal (KKR) adalah suatu penyakit yang dinamis dan heterogen sehingga untuk mengetahui perangai biologinya membutuhkan identifikasi mutasi gen. KKR melibatkan banyak variasi mutasi gen dan profilnya berbeda-beda antarindividu sehingga penting diketahui pada populasi spesifik. Indonesia hingga kini belum memiliki profil mutasi gen penderita keganasan kolorektal. Penelitian ini bertujuan untuk mendeskripsikan profil mutasi gen yang paling sering terlibat yaitu APC, TP53, PIK3CA, KRAS, dan MLH1 pada penderita KKR di 3 rumah sakit Jakarta. Metode : Penelitian ini adalah penelitian deskriptif yang dilakukan pada penderita KKR yang diberikan terapi bedah dan/atau neoadjuvan dan/atau adjuvan di RSCM, RSKJ, dan MRCCC tahun 2017-2018. Analisis DNA dilakukan dengan menggunakan next-generation sequencing dan disesuaikan dengan GRCh38. Varian patogenik diidentifikasi berdasarkan klasifikasi ACMG dan skor FATHMM. Data klinis dikumpulkan dari rekam medik. Hasil : Terdapat 22 total subjek dengan mutasi patogenik gen APC, TP53, dan PIK3CA yang terjadi 100%, KRAS 64%, dan MLH1 45%. Terjadi 5 jenis mutasi pada kelima gen tersebut yaitu nonsense, missense, frameshift, splice-site, dan silent. Terdapat 4 kelompok co-occurring mutation yang memiliki presentasi klinis berbeda, yaitu APC, TP53, dan PIK3CA (Triple Mutation/TM), TM+KRAS, TM+MLH1, TM+KRAS+MLH1. Kesimpulan : Populasi Indonesia, yang terdiri dari berbagai etnik dengan beragam pola makan dan gaya hidup, memiliki profil mutasi patogenik yang unik dibandingkan negara lain dengan presentasi klinis yang didominasi oleh stadium lokal lanjut dengan luaran dan sintasan yang bervariasi.
.....Background : Knowing colorectal cancer’s heterogeneity and dynamic features, recognizing its biological behaviour requires detailed identification of mutated genes involved. Colorectal cancer (CRC) requires several mutated genes to occur and those are dissimilar in each person hence essential to be discovered in specific population. Until recently, there is now known study describing genomic landscape of CRC in Indonesian population. This study aims to describe profile of pathogenic mutation of APC, TP53, PIK3CA, KRAS, and MLH1 in CRC patients treated at 3 different hospitals in Jakarta. Methods : This is a descriptive study conducted on CRC patients who underwent neoadjuvant, surgical, and adjuvant therapy at RSCM, RSKJ, and MRCCC in 2017-2018. DNA analysis was performed using next-generation sequencing and aligned against GRCh38. Pathogenic variant was identified using ACMG classification and FATHMM score. Data related to behaviour and survival were collected from medical records Results : There were total 22 subjects in which APC, TP53, and PIKCA were mutated. KRAS mutation occurred in 64%, while MLH1 in 45%. Five types of mutation were identified, including nonsense, missense, frameshift, splice-site, and silent mutation. There are 4 groups of co-occurring mutations, which are APC, TP53, PIK3CA (triple mutation/TM) alone; TM+KRAS; TM+MLH1; and TM+KRAS+MLH1, presenting different nature and survival. Conclusion : Indonesia having various ethnicities with diverse diet and lifestyle has distinct profile of pathogenic mutation presenting mostly with locally-advanced stage with various outcome and survival

rate.