

# Perbedaan ekspresi Beta-catenin pada faktor Prognosis Karsinoma Sel Hati: Studi pada Alfa-Fetoprotein, Derajat Diferensiasi dan Invasi Mikrovaskular = Beta-catenin expression and its association with prognostic factors in hepatocellular carcinoma: A study on alpha-fetoprotein, tumor grade and microvascular invasion

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## Abstrak

Latar belakang: Karsinoma sel hati (KSH) merupakan jenis keganasan primer hati tersering dengan gambaran histologik menunjukkan diferensiasi sel hepatoselular. Selain insiden yang tinggi, beban yang berat dari keganasan ini adalah prognosis yang sangat buruk dengan angka rekurensi yang tinggi. Terdapat banyak faktor resiko secara klinikopatologik yang telah diketahui mempengaruhi prognosis KSH, seperti kadar alfa fetoprotein, derajat diferensiasi, dan invasi mikrovaskular. Secara molekular, mutasi p53 dan -catenin merupakan dua mutasi tersering dalam KSH. -catenin merupakan protein multifungsi yang dikode oleh gen CTNNB1 yang dapat ditemukan pada 3 kompartemen sel, yaitu di membran sel, sitoplasma dan inti. Jalur Wnt/-catenin meregulasi proses seluler yang terkait inisiasi, pertumbuhan, survival, migrasi, diferensiasi, dan apoptosis. Meski sudah banyak diketahui beberapa jalur patofisiologi molekular hepatokarsinogenesis, hubungan dengan aplikasi klinik membutuhkan pemahaman lebih mengenai hubungan sifat molekuler dan sifat fenotip tumor, terutama dalam penentuan faktor prognosis dan pengembangan terapi target. Penelitian ini bertujuan untuk menilai ekspresi -catenin pada KSH dan hubungannya dengan berbagai faktor prognosis yaitu AFP, derajat diferensiasi dan invasi mikrovaskular.

Bahan dan cara: Penelitian ini menggunakan desain potong lintang. Sampel terdiri atas 35 kasus KSH yang sudah ditegakkan diagnosisnya berdasarkan pemeriksaan histopatologik dan/atau imunohistokimia di RSCM dari Januari 2013 sampai September 2019. Dilakukan pulasan -catenin dan analisis statistik dengan uji komparatif terhadap berbagai karakteristik klinikopatologik dan faktor resiko berupa AFP, derajat diferensiasi dan invasi mikrovaskular.

Hasil: Terdapat perbedaan bermakna ekspresi -catenin terhadap AFP ( $p=0,037$ ) dan derajat diferensiasi ( $p=0,043$ ) pada KSH. Ekspresi -catenin pada inti dengan/tanpa sitoplasma lebih sering ditemukan pada kasus KSH dengan kadar AFP rendah dan derajat diferensiasi baik-sedang. Tidak ditemukan perbedaan bermakna ekspresi -catenin terhadap invasi mikrovaskular pada KSH ( $p=1,000$ ).

Kesimpulan: Terdapat perbedaan bermakna ekspresi -catenin terhadap AFP dan derajat diferensiasi pada KSH.

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Background: Hepatocellular carcinoma (HCC) is the most common primary liver cancer, displaying histologically hepatocellular differentiation. In addition to its high

incidence, the disease burden of HCC is due to its poor prognosis with high recurrence rate. Some of the previously known clinicopathologic prognostic factors of HCC include alpha-fetoprotein (AFP) level, tumor grade and microvascular invasion. At molecular level, p53 and  $\beta$ -catenin are the two most common driver mutations in HCC that are mutually exclusive.  $\beta$ -catenin is a multifunction protein that is encoded by CTNNB1 gen. It is found in 3 compartments of cells, which are membrane cell, cytoplasm and nucleus. Wnt/  $\beta$ -catenin pathway regulates cellular process which is related to initiation, growth, survival, migration, differentiation and apoptosis. Although molecular pathogenesis pathways of hepatocarcinogenesis are known, clinical application warrants more understanding in terms of molecular characteristic and tumor phenotype, especially in determining prognosis and target therapy development. This current study aims to analyze the expression of  $\beta$ -catenin and its association with prognostic factors, such as AFP, tumor grade and microvascular invasion.

**Material and method:** A cross-sectional study was conducted comprising 35 samples of surgically resected HCCs between January 2013 to September 2019 in Cipto Mangunkusumo General Hospital. The cases were diagnosed based on histopathological and immunohistochemical findings and was then performed  $\beta$ -catenin staining.  $\beta$ -catenin expression was analyzed with statistical tests to determine expression difference between AFP level, tumor grade and microvascular invasion.

**Result:** There were statistically significant difference of  $\beta$ -catenin expression in AFP level and tumor grade ( $p=0.037$  and  $0.043$ , respectively). Nuclear with/without cytoplasmic expression of  $\beta$ -catenin was more frequently found in HCC with low AFP level and well-to-moderately differentiated tumors. No significant difference was observed in  $\beta$ -catenin expression between HCC with and without microvascular invasion ( $p=1.000$ ).

**Conclusion:**  $\beta$ -catenin expression was significantly different in AFP level and tumor grade.