Hepatocellular Carcinoma Serum Markers

Hepatocellular carcinoma (HCC) is the most common type of primary liver cancer in adults. Risk factors include hepatitis B or C infection, toxin exposure, metabolic or genetic disorders, hepatic steatosis, and cirrhosis. Ethnicity and age can also increase risk, especially when combined with other risk factors. Depending on staging, surgery (partial hepatectomy) or transplant are the main treatment options, although radiation and drug therapy may be used. Serum testing aids in surveillance and monitoring treatment progress and in determining prognosis.[1]

Featured ARUP Testing

Alpha Fetoprotein, Total and L3 Percent 0081208

Method: Quantitative Liquid Chromatography/Immunoassay

Surveillance and monitoring of HCC

Des-gamma-carboxy Prothrombin 0081312

Method: Quantitative Liquid Chromatography/Immunoassay

Surveillance and monitoring of HCC

Disease Overview

Prevalence and/or Incidence

- 4-11/100,000 (U.S. and Europe)
- >33,000 new cases per year[2]

Screening/Detection

- Disease is often discovered at late stage due to nonspecific symptoms
- Poor prognosis at this point
- Possible role for surveillance of high-risk individuals using combined serum marker testing and abdominal ultrasound to detect earlier disease

Biology

- Alpha-fetoprotein (AFP)-L3
  - AFP has 3 isoforms: L1, L2, L3
  - L3 isoform is expressed by malignant hepatocytes
  - L3 isoform has highest affinity for lectin from Lens culinaris, which makes it possible to differentiate L3 from other isoforms
- Des-gamma carboxyprothrombin (DCP)
  - Also referred to as PIVKA-II (protein induced by vitamin K absence or antagonist II)
  - Nonfunctional prothrombin
  - Results from lack of carboxylation of 10 glutamic acid residues
  - Vitamin K dependent carboxylase, which catalyzes this reaction in many HCCs, is absent

Test Interpretation

Sensitivity/Specificity

- Clinical sensitivity/specificity
  - AFP-L3%
    - L3% ≥10%
      - Relative risk (RR): 43.3% (95% confidence interval [CI]: 31.4-55.4%)
    - L3% <10%
      - RR: 4.1% (95% CI: 1.6-6.6%)

    - DCP
        - DCP ≥7.5
            - RR: 36.5% (95% CI: 23.5-49.6%)
        - DCP <7.5
            - RR: 7.6% (95% CI: 4.4-10.8%)
- Analytic sensitivity
    - AFP and DCP: 0.1 ng/mL
- Analytic specificity: none known

Results

- Normal cutoffs
    - AFP: 0-15 ng/mL
    - AFP-L3%: 0-9.9%
    - DCP: 0-7.4 ng/mL

Limitations

- Not all HCCs secrete AFP and/or DCP
    - Test is not useful for monitoring if pretreatment levels were not elevated
- False-positive result may occur in the following clinical contexts:
    - AFP-L3%
        - Pregnancy
        - Age <1 year
        - Acute fulminant hepatitis
        - Cirrhosis
        - AFP producing tumors other than HCC can show high values for AFP and AFP-L3%
        - Heterophilic antibodies
    - DCP
        - Obstructive jaundice
        - Intrahepatic cholestasis
        - Drugs (eg, warfarin)
        - DCP producing tumors other than HCC can show elevated values of DCP
        - Heterophilic antibodies

References

1. National Comprehensive Cancer Network: Clinical Practice Guidelines in Oncology: Hepatobiliary cancers. Version 4.2019. [Updated: Dec 2019; Accessed: Feb 2020]

2. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention. Liver cancer. [Last reviewed: Jul 2019; Accessed: Feb 2020]

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