

Des-gamma-carboxy Prothrombin

FOR RISK ASSESSMENT OF HEPATOCELLULAR CARCINOMA IN PATIENTS WITH CHRONIC LIVER DISEASE

Test Highlights

- Des- γ -carboxy prothrombin (DCP) is also known as protein induced by vitamin K absence or antagonist-II (PIVKA-II).
- DCP concentrations in serum are elevated in patients at increased risk for hepatocellular carcinoma (HCC).
- DCP in serum from patients with liver disease has a high specificity for HCC.
- Several studies have shown that DCP acts independently of other established HCC markers, such as alpha fetoprotein (AFP) or alpha fetoprotein L3 percent (AFP-L3%). It can therefore be used to complement these biomarkers in surveillance and risk assessment for HCC. In a prospective study of patients in the United States with an established diagnosis of HCC, the sensitivities for AFP, AFP-L3%, and DCP were 68%, 62%, and 73%, respectively. When the three markers were combined, the sensitivity was 86%.
- DCP values are closely related with disease progression and tumor size. DCP parallels the stage of HCC, and elevated levels have been associated with intra-hepatic metastases, tumor thrombus in the portal or hepatic vein, and invasion of tumor capsule. Elevated DCP is an indicator of poor prognosis.
- The high specificity of DCP makes it a useful marker for monitoring patients with HCC after therapy, if they were positive for this marker prior to therapy.

Clinical Background

- HCC incidence in the United States has increased substantially over the last few decades. Approximately 24,000 new cases occur every year. This highlights an increasing need for specific biomarkers to assist in risk assessment, surveillance, and early detection of HCC.
- The National Cancer Institute projects 3% to 5% annual increases in the prevalence of HCC.
- Patients with chronic hepatitis B or C, hemochromatosis, or cirrhosis are at highest risk for HCC.
- A 2010 Centers for Disease Control report found a total of 48,596 new cases of HCC during 2001–2006 and an average annual incidence rate of 3/100,000 persons.
- DCP is a nonfunctional prothrombin resulting from a lack of carboxylation of 10 glutamic acid residues in the N-terminal portion of the molecule. In normal prothrombin, a precursor undergoes post-translational carboxylation in the liver before being released into the peripheral blood. The vitamin K-dependent carboxylase responsible is absent in many HCC cells, which secrete the noncarboxylated form, DCP.
- This FDA-cleared test measures DCP in ng/mL. In clinical studies of patients with liver disease, a decision cutoff level of 7.5 ng/mL was found to be optimal, giving a minimum relative risk of 4.8 for HCC. The sensitivity and the specificity for DCP were 49% and 88%, respectively; the negative predictive value for HCC was 92%.
- A 2008 study demonstrated that DCP should be utilized for HCC surveillance. Compared to AFP and AFP-L3%, DCP had the highest sensitivity (87%) and the highest positive predictive value (87%) in patients with HCC due to chronic hepatitis B and C infections.

Limitations

- DCP can be detected at high concentrations in other conditions besides HCC. These include obstructive jaundice, intrahepatic cholestasis causing chronic decrease in vitamin K, and ingestion of drugs such as warfarin or wide-spectrum antibiotics. Because of this, DCP values do not necessarily reflect HCC burden in patients with persistent jaundice or deficient concentrations of vitamin K due to malnutrition.
- Not all liver cancers secrete DCP. Between one-quarter and one-half of patients with HCC will have a negative result for DCP.

Methodology

The μ TASWako[®] DCP assay uses a microfluidic electrophoretic separation process on a chip. The sample and antibody reagents are dispensed into the chip and form the primary immunocomplex. Voltage is applied to the chip, and a DNA-labeled secondary antibody moves to the anode and is concentrated by isotachopheresis. This concentrated secondary antibody reacts with the primary immunocomplex and forms the secondary immunocomplex. This secondary immunocomplex is further concentrated during isotachopheresis to the anode and is separated from unbound reagent by capillary gel electrophoresis. The signal from the immunocomplex is detected by laser-induced fluorescence and is proportional to the concentration of DCP.

Related Tests

- Alpha Fetoprotein, Serum (Tumor Marker) ([0080428](#))
- Alpha Fetoprotein, Total and L3 Percent ([0081208](#))
- Hepatocellular Carcinoma Tumor Marker Panel ([0081326](#))

References

1. Hakamada K, et al. Des-gamma-carboxy prothrombin as an important prognostic indicator in patients with small hepatocellular carcinoma. *World J Gastroenterol*. 2008;14(9):1370–1377.
2. Carr B, et al. Clinical evaluation of Lens culinaris agglutinin-reactive alpha-fetoprotein and des-gamma-carboxy prothrombin in histologically proven hepatocellular carcinoma in the United States. *Dig Dis Sci*. 2007;52:776–782.
3. Cabibbo G, Craxi A. Hepatocellular cancer: optimal strategies for screening and surveillance. *Dig Dis*. 2009;27(2):142–147.
4. Donati M, Brancato G, Donati A. Clinical biomarkers in hepatocellular carcinoma (HCC). *Front Biosci*. (Schol Ed). 2010;2:571–577.

Test Information

0081312

Des-gamma-carboxy Prothrombin

For specific collection, transport, and testing information, refer to the ARUP website at www.aruplab.com.

For information on test selection, ordering, and interpretation, refer to ARUP Consult® at www.arupconsult.com.

AUTHORS

David G. Grenache, PhD

Shawn R. Clinton, PhD