

DCP:

A Complementary Biomarker for HCC

INTRODUCTION

There is a need for specific biomarkers to aid in risk assessment, surveillance and early diagnosis of hepatocellular carcinoma (HCC).¹ Early detection is critical for improved prognosis², and the rising incidence of HCC intensifies the need for earlier diagnosis. Wako introduces a third serum marker in its HCC Panel: des-γ-carboxy prothrombin (DCP) also known as PIVKA-II (protein induced by vitamin K absence-II). Wako's DCP assay is FDA cleared for clinical use as a risk assessment test for the development of HCC in patients with chronic liver diseases. It complements the other established HCC biomarkers, AFP and AFP-L3% in HCC surveillance and risk assessment.

WHAT IS DCP?

DCP is an abnormal form of the coagulation protein, prothrombin. The prothrombin precursor undergoes post-translational carboxylation in the liver prior to secretion into plasma. Many HCCs lack the responsible carboxylase and these HCC cells instead secrete the unmodified precursor, DCP. DCP lacks thrombotic activity and has been shown in multiple studies to be present in the serum of patients with HCC. AFP and DCP are different and independent tools for the risk assessment, surveillance and detection of HCC.

THE DIAGNOSTIC PERFORMANCE OF DCP

The diagnostic sensitivity and specificity of any test depend on the cut off value selected and the type of patients included. The diagnostic sensitivity of DCP in 6 cross-sectional studies has varied from 28% to 89% and in 5 prospective studies from 7% to 57%.³

Adoption of an assay into a surveillance program or in enhanced follow-up requires high specificity and high Negative Predictive Value. The Wako DCP test was characterized in a prospective study of 332 North American patients with HCV cirrhosis. Using a 7.5 ng/mL cutoff (selected to maximize relative risk at 5.7) the Wako DCP assay gave a diagnostic specificity of 91% and a Negative Predictive Value of 93% (Table 1).⁴ The sensitivity of 49% reflects the fact that there is no single specific marker expressed by all HCCs. With this same patient population, a 2.5 ng/mL cutoff value gave a sensitivity of 67% and a Negative Predictive Value of 91%. Other studies support the finding that DCP is a reproducible test with excellent analytical sensitivity and excellent analytical specificity for HCC (please contact Wako Diagnostics for support information).

	DCP cutoff value: (ng/mL)	
	2.5	7.5
Relative Risk	4.0	5.7
Positive Predictive Value	34%	42%
Negative Predictive Value	91%	93%
Sensitivity	67%	49%
Specificity	74%	91%

Table 1: DCP Assay Performance is a Function of the Cutoff Value
Sterling et al. (2007) prospectively evaluated 332 patients with HCV cirrhosis, of whom 34 developed HCC.⁴ The conversion is 1 ng= 52.6 mAU purified des-γ-carboxy prothrombin. Wako's DCP results are determined on the fully automated LIBASys (Liquid-phase Binding Assay system) instrument.⁵

DCP IS EXPRESSED INDEPENDENTLY OF AFP AND AFP-L3%

Several studies using AFP, AFP-L3% and DCP in HCC patients have shown that the expression of these 3 biomarkers is only partially overlapping.^{4,6} In patients with early stage or recently diagnosed HCC, no one marker is found in all patients, many patients have only one marker and some patients lack any of these 3 markers. Toyoda et al. studied the differential expression of AFP, AFP-L3% and DCP in 685 patients at the time of diagnosis of HCC.⁶ In this study, the sensitivity of DCP was 54%, and of AFP-L3% was 34%. Figure 1 describes the results for AFP and DCP. There were 125 patients (18%) who were detected by DCP but not by AFP.

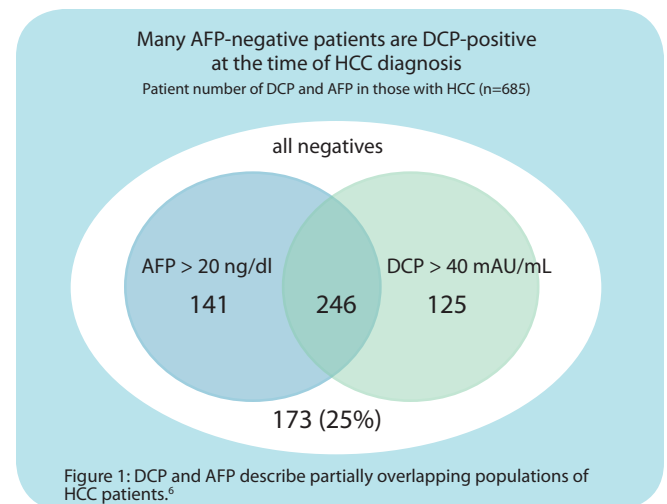


Figure 1: DCP and AFP describe partially overlapping populations of HCC patients.⁶

DIFFERENTIATION OF HCC USING DCP

Patients who test positive for DCP often show features of HCC that are different from those who test positive for AFP-L3.⁶ The differential expression of these biomarkers coincides with different HCC tumor characteristics. Numerous published studies show that DCP elevation reflects the progression of the disease and the tumor diameter.⁷ Koike et al. reported that DCP was the most significant predisposing factor for the development of portal vein invasion (PVI), an indicator of end stage liver disease.⁸ Okuda et al. reported that HCC patients with elevated DCP and normal AFP tend to have more advanced HCC.⁹ The combined use of the three biomarkers offers stronger discrimination between benign and malignant conditions related to primary liver disease.¹⁰

WAKO'S HCC TESTS

Routine evaluation of risk for patients with chronic viral hepatitis and/or cirrhosis should include the use of DCP with AFP and AFP-L3%.⁶ AFP-L3% and DCP are available through major reference labs. DCP and AFP-L3% have received 510(k) clearance approval from the FDA as risk assessment tests for the development of HCC. For additional information regarding DCP, the assay or to locate a testing lab, please contact Wako Diagnostics: 877-714-1924 (t) or liver@wakousa.com.

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