**Multi-biomarker Panels for the Identification of Hepatocellular Carcinoma**

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**Abstract**

*Introduction*

Biomarker combinations such as the GALAD, GAAD and HES scores have been proposed to aid detection of hepatocellular carcinoma (HCC), a common, debilitating primary liver cancer. A method is required to assess and compare the accuracy of the various combinations that are available.

*Methods*

Predictive models were developed using logistic regression based on data from several large previously published datasets; for all 31 possible combinations of five biomarkers – alpha-fetoprotein (AFP), *Lens culinaris* agglutinin-reactive AFP (AFP-L3), des-gamma-carboxy prothrombin (DCP), age and sex – area under the curve (AUC), sensitivity and specificity scores were generated to estimate HCC diagnostic performance.

*Results*

DCP was the most important single biomarker for predicting HCC (AUC=0.89). AFP was the second most important biomarker; combining DCP and AFP produced an AUC of 0.94. Addition of the third most important biomarker significantly improved AUC, as did addition of the fourth but there was no significant difference in AUC between the 4-biomarker and full 5-biomarker models.

*Conclusions*

Our work suggests that biomarker combinations can be flexible to accommodate individual patient and healthcare provider needs. There is no statistical difference between the 4- and 5-biomarker models, indicating that the GALAD score is simply one of a family of models, all with similar performance characteristics. Our automated calculator easily assesses the AUC of all possible biomarker combinations and can be applied to biomarkers in other disease areas.