The ‘GALAD score’ for the serological detection of hepatocellular carcinoma: international validation and assessment of the influence of tumour size and aetiology on model utility

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BACKGROUND

A statistical model, developed in the UK, permits estimation of the likelihood that hepatocellular carcinoma (HCC) is present in individual patients with chronic liver disease (CLD) using objective measures, particularly the serological tumour markers (AFP, AFP-L3 and DCP).

This model (1), which has the potential to be used in the screening/surveillance setting, has not been validated in an international setting.

OBJECTIVES

To validate the model in an international setting by application to cohorts from Japan and Germany.

To compare the model with one where the biomarkers are used individually or to the conventional approach of using these biomarkers in the Japanese screening program.

Assess the influence of aetiology and tumour size on model utility.

MATERIALS & METHODS

Cohorts comprising 4476 patients from Ogaki, Japan (1514 HCCs and 2962 CLDs) and 1086 from three centres in Germany, namely Hannover, Leipzig and Essen (238 HCCs and 848 CLDs) were recruited.

We also included, for reference, the original UK cohort on which the model was developed (394 HCCs and 439 CLDs) (1). We assessed the change in sensitivity, specificity and area under the ROC curve (AUROC).

In each case sera and related clinical features were collected by investigators independent of the laboratory (Wako Life Sciences, Inc.) in which the biomarker assays were performed and the group performing the statistical analysis.

RESULTS

Table 1: Demographics of the cohorts involved in validation of the model.

Figure and Table 2: In all three cohorts, the figures for the optimised sensitivity and specificity (Table 2), and the AUROC derived from the model (Figures 2a, 2b and 2c) were superior to those obtained if the biomarkers were used individually or combined (as currently used in clinical practice in Japan).

Figure and Table 3: Within each cohort, the utility of the model was only slightly lower in the smaller tumours (Figure 3a, 3b and 3c). This is demonstrated by the fall in AUROC value if tumor size was categorized from <5cm to <5cm. There was also no significant change in model performance between HBV, HCV and other subgroups, in all three cohorts. The model performed well in all three aetiologies (Figure 3d, 3e and 3f). Sensitivity and specificity data are shown in Table 3.

SUMMARY

GALAD model performance on the validation cohorts was very similar to that obtained in the original UK dataset.

Model utility was better than using the biomarkers individually.

Model utility was slightly reduced in smaller tumours, but unaffected in the different aetiologies.

CONCLUSIONS

The GALAD model for serological diagnosis of HCC has been validated by application to patient cohorts from Germany and Japan.

Having validated the model, its potential role in a clinical surveillance setting will need to be assessed.

REFERENCES


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