Artificial intelligence predicts outcome-related molecular profiles and vascular invasion in hepatocellular carcinoma

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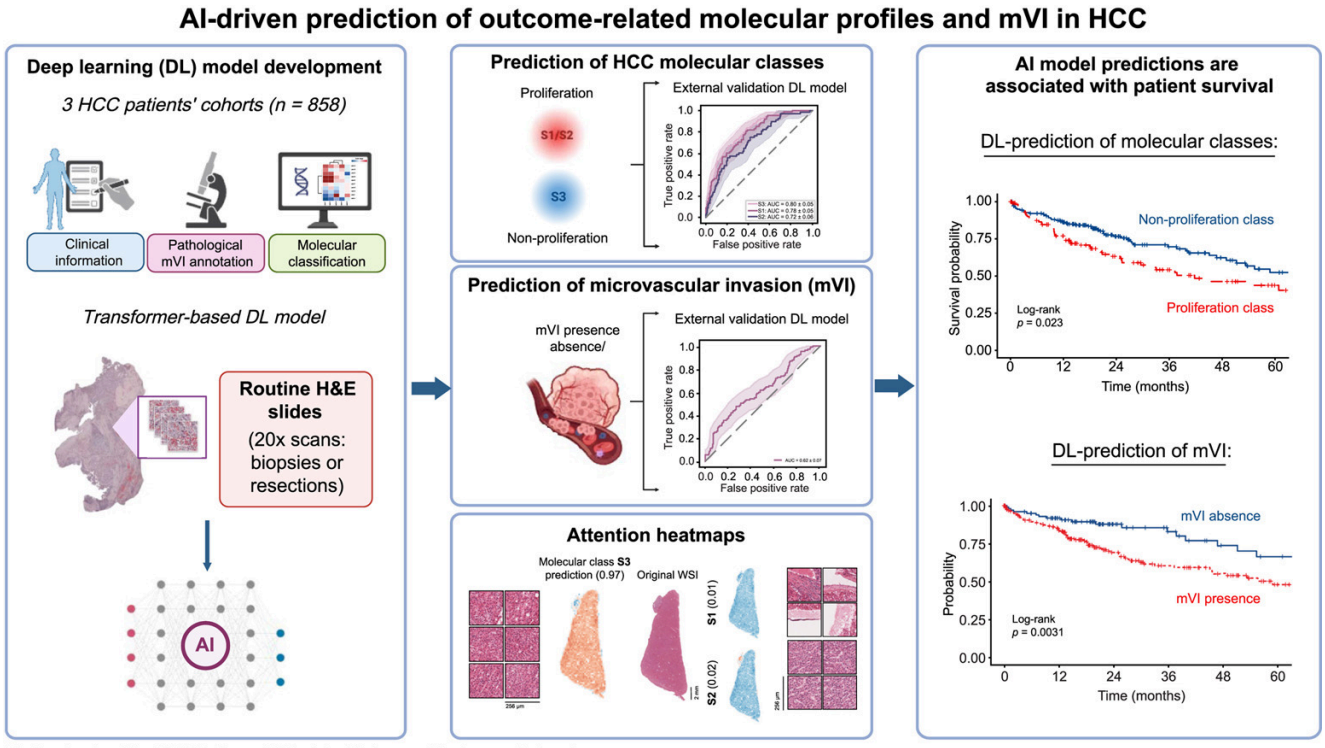
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Autoren

Tobias Paul Seraphin Agavni Mesropian Laura Žigutytė James Brooks Ezequiel Mauro Albert Gris-Oliver Roser Pinyol Carla Montironi Ugne Balaseviciute Marta Piqué-Gili Júlia Huguet-Pradell Marko van Treeck Michael Kallenbach Anne Theres Schneider Christoph Roderburg Jakob Nikolas Kather Tom Luedde Josep M. Llovet



DL, deep learning; AI, artificial intelligence; WSI, whole-slide image; mVI, microvascular invasion

Abstract

Background & Aims

Advances in digital pathology and artificial intelligence (AI) are driving progress toward personalized clinical management. In hepatocellular carcinoma (HCC), AI-based models using digitized H&E slides can be a robust tool to predict outcome-related molecular profiles and presence of microvascular invasion (mVI), with potential clinical utility.

Methods

A transformer-based deep-learning (DL) model was deployed using digitized H&E slides from 431 resected HCC cases (training cohort). Five-fold cross-validation was applied, and the model was tested on two external cohorts: TCGA-LIHC (n = 363) and advanced-stage HCC cohort (n = 64).

Results

The DL model effectively predicted outcome-related molecular profiles, distinguishing poor-prognosis (S1/S2, proliferation) from good-prognosis (S3, non-proliferation) subclasses. In internal cross-validation, mean areas under the curves (AUCs) were 0.75 for proliferation and 0.79 for non-proliferation subclasses. This performance was reproduced in the TCGA test set, with AUCs ranging from 0.72–0.80, and in the advanced-stage HCC cohort, with AUCs ranging from 0.76–0.81. In these test sets, the AI-predicted non-proliferation subclass was associated with a longer median OS compared with the proliferation subclass (5.8 vs. 3.5 years in TCGA; p = 0.02). For mVI prediction, the DL model achieved a mean AUC of 0.70 in the internal cross-validation and 0.62 in the TCGA. AI-predicted mVI was associated with shorter OS (4.9 vs. 7.6 years for non-mVI; p = 0.003) and an immunosuppressive microenvironment (p = 0.002).

Conclusions

Our H&E-based AI model enables accurate prediction of outcome-related molecular subtypes of poor prognosis and presence of mVI, offering a scalable and accessible tool to extract clinically relevant features from routine histology.

Impact and implications

Outcome-related molecular profiles and the presence of microvascular invasion (mVI) are critical determinants of prognosis and treatment decisions in hepatocellular carcinoma (HCC). This study presents an artificial intelligence (AI)-based method that analyzes routine H&E-stained slides and accurately predicts: (a) biologically relevant HCC molecular subtypes associated with patient outcomes, and (b) the presence of mVI, a well-established predictor of poor outcomes and risk of recurrence, that currently requires meticulous pathological assessment of multiple H&E slides. These AI tools can offer a scalable method to support personalized treatment decisions, such as transplant eligibility, trial enrollment, or neo/adjuvant therapy planning, and may improve clinical management of HCC. Our findings lay the groundwork for incorporating AI-assisted pathology into future prospective studies aimed at improving HCC clinical management.