Enhancing prediction of moderate fibrosis in MASLD patients for Resmetirom treatment via machine learning


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Background and Aims:
Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) affects approximately 30% of the global adult population and poses significant risks of disease progression, particularly in patients with moderate to advanced fibrosis (stages 2-3). Following the FDA’s approval of Resmetirom for treating Metabolic Dysfunction-Associated Steatohepatitis (MASH) in these stages, there is a need for a surrogate marker to refine the selection of patients for liver biopsy. The ALADDIN study introduces a novel machine learning-based web calculator to estimate the probability of stage ≥2 fibrosis in MASLD using routine laboratory parameters, with and without Vibration Controlled Transient Elastography (VCTE).

Method:
A total of 3708 patients with biopsy-confirmed MASLD from six centers worldwide were divided into Derivation and Internal Validation cohorts on a 1:1 basis, supplemented by 1289 patients from nine centers for External Validation. ALADDIN models, employing Random Forest, Gradient Boosting Machines, and XGBoost enhanced by Bayesian updates, were developed to evaluate moderate fibrosis (stage ≥F2).

Results:
The VCTE model achieved an Area Under the Curve (AUC) of 0.800 (95% CI 0.773-0.827) in external validation, significantly outperforming the FAST (AUC: 0.707, 95% CI 0.674-0.739, p<0.0001) and Agile-3 (AUC: 0.764, 95% CI 0.735-0.793, p=0.001) models. The model using routine laboratory parameters without VCTE reached an AUC of 0.757 (95% CI 0.730-0.783), comparable to FAST and Agile-3. The VCTE model model also demonstrated superior decision curve analysis, calibration, and classification accuracy, using a dual cut-off approach, and outperformed existing models in predicting moderate fibrosis.

Conclusion:
The ALADDIN study, via an international consortium, has successfully developed and externally validated machine learning models that predict moderate fibrosis with notable accuracy. Our VCTE model, available at https://aihepatology.shinyapps.io/ALADDIN1/, and our routine laboratory parameter model without VCTE, available at https://aihepatology.shinyapps.io/ALADDIN2/, demonstrate statistical superiority and comparable performance, respectively, against traditional models including Agile-3 and FAST. These algorithms will facilitate targeted liver biopsy in line with the new FDA approval for Resmetirom treatment.