Supplementary Table 1. Model development and test dataset characteristics.

Dataset	Trial phase	Number of WSIs (H&E, MT)	Drug class	Enrollment criteria
Model development datasets				
1	3	2188, 2188	ASK1 inhibitor	NASH diagnosis; fibrosis F3[23]
2	3	2488, 2478	ASK1 inhibitor	NASH diagnosis; fibrosis F4[23]
3	2b	528, 528	Monoclonal antibody directed against LOXL2	NASH defined as steatosis > 5% with associated lobular inflammation: Ishak stage 3,4[47]
4	2b	561, 554	Monoclonal antibody directed against LOXL2	NASH diagnosis; Ishak stage 5,6[21]
5	2	158, 163	ASK1 Inhibitor, monoclonal antibody directed against LOXL2	Evidence of NASH with fibrosis on biopsy[48]
6	2	312, 312	PPARδ agonist	Definite NASH; NAS ≥ 4 with 1 per component; fibrosis F1, F2, F3[49]
7	3	1477, 766	Nucleotide analogue (antiviral)	HBV[50]
8	3	851, 415	Nucleotide analogue (antiviral)	HBV[50]
9	2b	331, 333	Monoclonal antibody directed against LOXL2	PSC[24]
Analytic performance test set				
10	2b	639, 633	Insulin sensitizer	Definite NASH; NAS ≥ 4 with 1 per component; Fibrosis F1, F2, F3[22]

ASK1, apoptosis signal-regulating kinase 1 (also known as mitogen-activated protein kinase kinase kinase 5); F, fibrosis stage; HBV, hepatitis B virus; H&E, hematoxylin and eosin; LOXL2, lysyl oxidase-like 2; MT, Masson's trichrome; NAS, NAFLD activity score; NASH, nonalcoholic steatohepatitis; PPARδ, peroxisome proliferator activated receptor delta; PSC, primary sclerosing cholangitis; WSI, whole slide image.

Supplementary Table 2. Algorithm repeatability assessment using 10 independent reads per WSI.

	Number of WSIs	Model versus model agreement rate
Steatosis	639	100%
Lobular inflammation	639	100%
Ballooning	639	100%
Fibrosis	633	100%

WSI, whole slide image.

Supplementary Table 3. Correlations between the AI-derived continuous scoring system and comparable noninvasive tests.

Continuous scoring system	NIT	Kendall's Tau	*P* value	*n*
Continuous fibrosis stage	FibroScan	0.33	2.49E–11	188
Continuous fibrosis stage	FIB4	0.23	1.56E–06	207
Continuous fibrosis stage	ELF	0.22	2.52E–06	210
Continuous fibrosis stage	TIMP1	0.11	2.01E–02	210
Continuous fibrosis stage	PIIINP	0.14	3.03E–03	210
Continuous fibrosis stage	MRI-PDFF	–0.11	2.36E–01	59
Continuous fibrosis stage	Morphometric quantitative collagen (%)	0.56	2.20E–32	205
Continuous steatosis grade	MRI-PDFF	0.52	4.83E–09	59
Continuous steatosis grade	Morphometric quantitative collagen (%)	–0.16	5.42E–04	205
Continuous lobular inflammation grade	C-reactive protein	0.13	5.04E–03	211
Continuous lobular inflammation grade	Adiponectin	–0.15	1.38E–03	211
Continuous ballooning grade	HbA1C	0.16	8.36E–04	211

AI, artificial intelligence; ELF, enhanced liver fibrosis test; FIB4, fibrosis-4; HbA1C, hemoglobin A1c; MRI-PDFF, magnetic resonance imaging derived proton density fat fraction; NIT, noninvasive test; PIIINP, procollagen III N-terminal peptide; Kendall's Tau, Kendall's rank correlation coefficient for ordinal scores; TIMP, tissue inhibitor of metalloproteinase; TIMP1, TIMP metallopeptidase inhibitor 1.

Supplementary Table 4. Example instructions for the interpretation of histologic features.

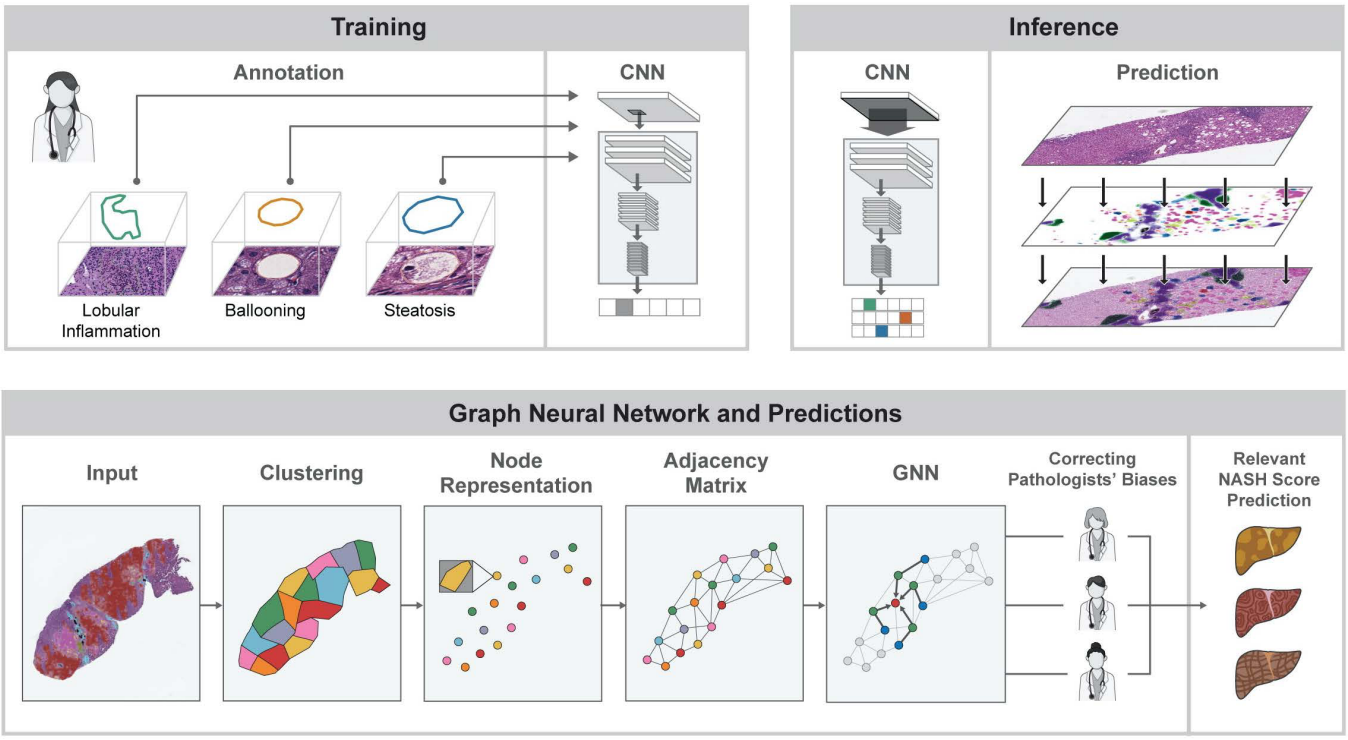
Histologic feature	Example instructions
Lobular inflammation	Place label regions containing at least three inflammatory cells, not including those within sinusoids. Do not label regions of portal inflammation with this region label.
Hepatocyte ballooning	Please use this label on regions of hepatocellular ballooning. Hepatocellular ballooning is defined as round cells with rarified cytoplasm that are at least 50% larger than neighboring normal cells.
Steatosis	Please use this label on regions of dense steatosis.
Thick pathologic fibrotic septa	Please use this label for thickened fibrotic septae extending from portal and central regions considered when staging liver biopsies.
Portal tract (normal)	Please use this label for normal-appearing, small-/medium-sized portal regions, not expanded by fibrosis or inflammation.
Portal tract (abnormal)	Please use this label for portal regions expanded by inflammation, fibrosis, bile ductular proliferation, or any combination of the above.
Large normal septa	Please use this label for larger intrahepatic normal septae (usually containing larger arteries, veins, and bile ducts) that would not be included when staging liver biopsies.
Subcapsular fibrosis	Please use this label for normal subcapsular regions of fibrosis not considered when staging liver biopsies.

Supplementary Table 5. AI-derived models, input substances, and objectives for application.

Model name	Major input substances	Objectives
Artifact model	Background, blur artifact, bad stain artifact, black spots, bubble, cautery, crushed tissue, hair, margin ink, marker tape, skin cell, tissue fold, rainbow pattern artifact	Remove unwanted regions of WSI that should be excluded from downstream analysis
MT tissue model	Lumen, blood vessel, bile duct, cirrhotic septal portal fibrosis, hilar fibrosis, large septal area, perisinusoidal fibrosis, septal fibrosis, subcapsular fibrosis, thick fibrotic septae, normal portal area, normal portal triad, fibrosis	Detect fibrosis regions to identify and quantify features of interest
MT large septae model	Normal portal area, normal portal triad, perisinusoidal fibrosis, thick fibrotic septae	Detect regions of pathological fibrosis
H&E tissue model	Lobular Inflammation, portal inflammation, interface hepatitis, bile duct, blood vessel, Normal hepatocytes, hepatocellular swelling, hepatocellular ballooning, steatosis, microvesicular steatosis	Detect macrovesicular steatosis, hepatocellular ballooning, and lobular inflammation regions to identify and quantify features of interest
H&E GNN model	*Overlays from H&E tissue model*: Lobular inflammation, portal inflammation, interface hepatitis, bile duct, blood vessel, normal hepatocytes, hepatocellular, swelling, hepatocellular ballooning, steatosis, microvesicular steatosis	Compute slide-level NASH CRN ordinal grades
MT GNN model	*Overlays from MT large septae model:* Large septae, pathological fibrosis, other tissue *Overlays from MT tissue model:* Fibrosis, bile duct, blood vessel, other tissue	Compute slide-level NASH CRN ordinal stage

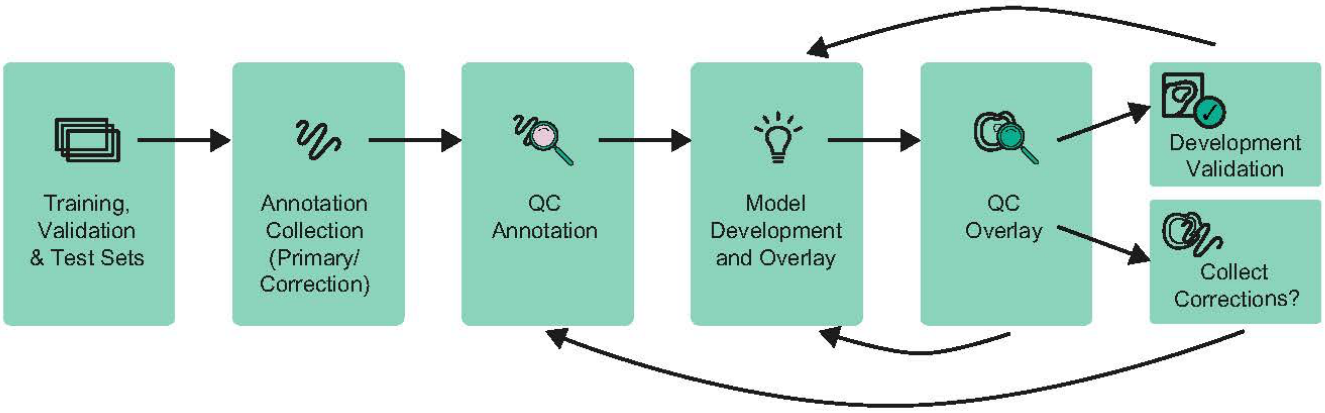
AI, artificial intelligence; CRN, Clinical Research Network; GNN, graph neural network; H&E, hematoxylin and eosin; MT, Masson's trichrome; NAS, nonalcoholic fatty liver disease activity score; NASH, nonalcoholic steatohepatitis; WSI, whole slide image.

Supplementary Fig. 1. Model training schematic.



CNN, convolutional neural network; GNN, graph neural network; NASH, nonalcoholic steatohepatitis.

Supplementary Fig. 2. Segmentation model development process.



QC, quality control.

Supplementary Fig. 3. Mapping of continuous scores.