A Deep Learning Approach to Analysis of MRCP Images Predicts Clinical Events and Progression to Cirrhosis in Patients With Primary Sclerosing Cholangitis

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Introduction

- Primary sclerosing cholangitis (PSC) is a chronic heterogeneous cholangiopathy and prognostic scores have modest ability to predict clinical outcomes[1,2]
- Magnetic resonance cholangiopancreatography (MRCP) is the primary method of PSC diagnosis, but its prognostic utility remains unclear[3,4]

Objectives

- To develop a machine learning (ML) algorithm based on MRCP images and evaluate its ability to predict clinical outcomes in patients with PSC enrolled in a clinical trial

Methods

- Baseline MRCP and liver biopsy images were available from patients (N=122) with compensated PSC enrolled in a 96-wk, Phase 2b clinical trial of simtuzumab (ClinicalTrials.gov NCT01672853)[5]
- A state-of-the-art, multilayer, convolution neural network (CNN) pretrained on ImageNet images was applied to the MRCP volumes[6]
- Activation maps generated from MRCP slices to a CNN were trained and cross-validated on a binary outcome of PSC-related clinical events (eg, hepatic decompensation, ascending cholangitis, and cholangiocarcinoma)
- The activation maps were input into a random forest classifier to generate ML MRCP scores; these scores were used for predicting progression to cirrhosis or development of PSC-related clinical events
- Discrimination of the resultant ML MRCP scores at baseline (range 0–1) for PSC-related clinical events and histologic progression to cirrhosis was determined using areas under receiver operating characteristic curves (AUROCs) and compared with other clinical parameters, including a semiquantitative MRCP risk score,[7] Ishak fibrosis stage, collagen proportionate area (CPA), serum alkaline phosphatase (ALP), Enhanced Liver Fibrosis (ELF™; Siemens Healthcare GmbH, Erlangen, Germany) score, Mayo risk score, PSC risk estimate tool (PREsTo) algorithm, and ML-based histologic features (PathAI, Inc., Boston, Massachusetts, USA)[8]

Results

Baseline Characteristics*

		N=122
Demographics	Age, y	45 (38, 52)
	Men	77 (63)
	BMI, kg/m^2	25.8 (23.5, 29.3)
	UDCA use	63 (52)
	Ulcerative colitis	63 (52)
Ishak Fibrosis Stage	F0–F2	56 (46)
	F3–F4	49 (40)
	F5–F6	17 (14)
Liver Tests	ALP, U/L	265 (126, 455)
	GGT, U/L	329 (105, 643)
	ALT, U/L	67 (35, 117)
	Bilirubin, mg/dL	0.7 (0.5, 1.1)
	Albumin, g/dL	4.0 (3.6, 4.2)
	INR	1.0 (0.9, 1.0)
	Platelets, x10^3/µL	245 (196, 302)

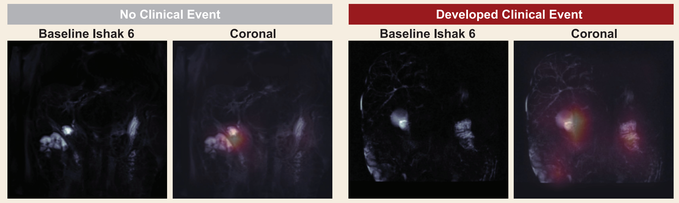
*Data are presented as median (quartiles 1, 3) or n (%). ALT, alanine aminotransferase; BMI, body mass index; GGT, γ-glutamyltransferase; INR, international normalized ratio; UDCA, ursodeoxycholic acid.

PSC-Related Clinical Events

	N=122
Clinical events, n (%)	25 (20)
Cholangitis	14 (11)
Jaundice	4 (3)
Ascites	2 (2)
Hepatic encephalopathy	2 (2)
Esophageal varices hemorrhage	2 (2)
Cholangiocarcinoma	1 (1)

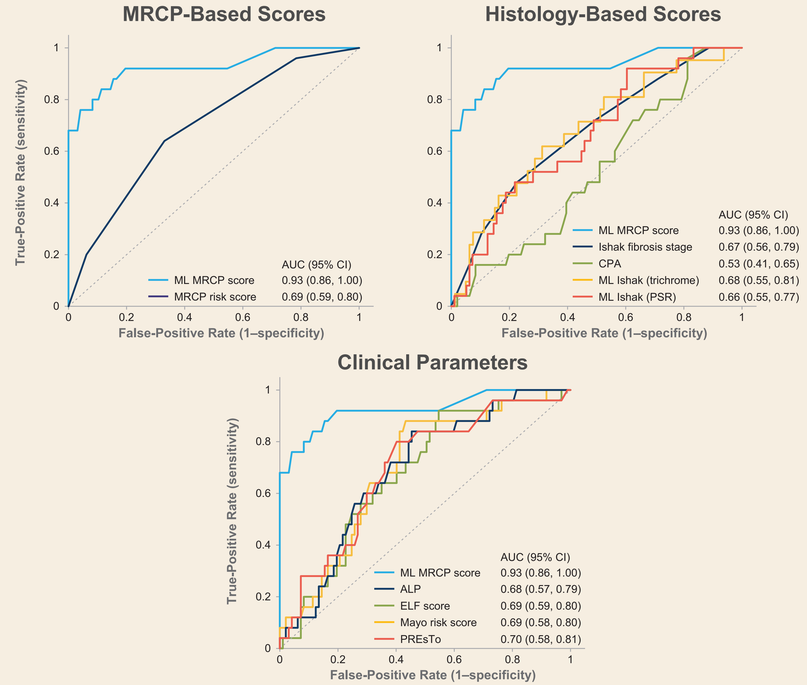
- During a median follow-up of 23.0 months (range 0.5–24.7), 25/122 patients (20%) had a PSC-related clinical event
- In all, 18/105 patients (17%) progressed to cirrhosis

CNN-Generated "Activation Maps" of MRCP Images Trained on Clinical Events*



*Activation maps of MRCP *images* of 2 patients with cirrhosis at baseline without and with development of clinical event.

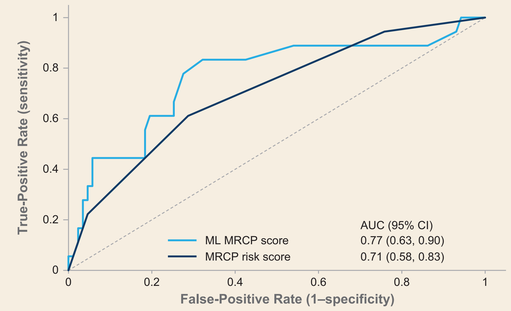
ML MRCP Score Was Superior to Clinical Parameters and Other Prognostic Models in Predicting PSC-Related Clinical Events



AUC, area under curve; CI, confidence interval; PSR, Picrosirius red.

- ML MRCP was superior to non-ML-based MRCP scores, and other clinical and histologic parameters

Discrimination of ML MRCP Score for Prediction of Progression to Cirrhosis



Discrimination of MRCP-Based Scores, Histologic Features, and Clinical Parameters for Clinical Events and Progression to Cirrhosis

		PSC-Related Clinical Events N=122		Progression to Cirrhosis n=105	
	Parameter	AUROC (95% CI)	p-Value vs ML MRCP Score	AUROC (95% CI)	p-Value vs ML MRCP Score
MRCP-Based Scores	ML MRCP score	0.93 (0.86, 1.00)	—	0.77 (0.63, 0.90)	—
	MRCP risk score	0.69 (0.59, 0.80)	<0.001	0.71 (0.58, 0.83)	0.54
Fibrosis	Ishak fibrosis stage	0.67 (0.56, 0.79)	<0.001	0.71 (0.59, 0.84)	0.61
	CPA	0.53 (0.41, 0.65)	<0.001	0.68 (0.55, 0.82)	0.47
	ML Ishak score (trichrome)	0.68 (0.55, 0.81)	<0.001	0.85 (0.74, 0.96)	0.28
	ML Ishak score (PSR)	0.66 (0.55, 0.77)	<0.001	0.75 (0.63, 0.86)	0.85
Clinical Parameters	ALP	0.68 (0.57, 0.79)	<0.001	0.75 (0.66, 0.85)	0.90
	ELF score	0.69 (0.59, 0.80)	<0.001	0.78 (0.67, 0.90)	0.84
	Mayo risk score	0.69 (0.58, 0.80)	<0.001	0.69 (0.53, 0.84)	0.48
	PREsTo	0.70 (0.58, 0.81)	<0.001	0.69 (0.53, 0.84)	0.50

ML MRCP Score Correlated Poorly to MRCP Risk Score, Clinical Parameters, and Other Prognostic Scores at Baseline

		ML MRCP Score (trained for clinical event) N=122	
	Parameter	Correlation Coefficient	p-Value
MRCP-Based Scores	MRCP risk score	-0.2025	0.025
Fibrosis	Ishak fibrosis stage	-0.1348	0.14
	% collagen morphometry	0.0252	0.78
	ML Ishak score (trichrome)	-0.1806	0.07
	ML Ishak score (PSR)	-0.1673	0.07
Clinical Parameters	ALP	-0.1524	0.09
	ELF score	-0.1848	0.042
	Mayo risk score	-0.1288	0.16
	PREsTo	-0.1902	0.036

Conclusions

- A deep learning approach to MRCP image analysis predicted clinical events in patients with PSC, and its prognostic utility exceeded that of other radiographic, clinical, and histologic assessments
- Further validation of these findings may provide a quantitative, ML-based assessment of PSC-related prognosis based on routinely collected MRCP images

References: **1.** Eaton JE, et al. Hepatology 2020;71:214-24; **2.** Goode E, et al. Hepatology 2019;69:2120-35; **3.** Lemoinne S, et al. Clin Gastroenterol Hepatol 2019;17:2785-92; **4.** Ruiz A, et al. Hepatology 2014;59:242-50; **5.** Muir A, et al. Hepatology 2019:69:684-98; **6.** Hu J, et al. 2018 IEEE/CVF Conference on Computer Vision and Pattern Recognition 2018:7132-41; **7.** Muir A, et al. AASLD 2017, poster 279; **8.** Travis N, et al. EASL 2020, poster FRI173.
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