Development of Machine Learning Histological Scores that Correlated with Portal Pressures and Development of Varices in NASH patients with Cirrhosis

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INTRODUCTION

- Primary endpoints of NASH cirrhotic trials include hepatic venous pressure gradient (HVPG) and liver histology.
- Reduction in HVPG and fibrosis improvement are associated with improved clinical outcomes.
- Current histological scoring systems do not capture septum thickness and nodule size as part of fibrosis dynamics in NASH cirrhosis.
- We examine if a machine learning (ML) algorithm can accurately predict HVPG and presence of varices from liver histology.

MATERIALS AND METHODS

- NASH patients with compensated cirrhosis and HVPG ≥ 6 mmHg (n=143) were included from Belapectin Phase IIa trial.[1]
- Baseline (BL) and end-of-treatment (EOT) liver biopsies, HVPG measurements and upper endoscopies were available.
- Second harmonic generation/two-photon excitation fluorescence (SHG/TPE) imaging-based tool provided quantitative assessment of **s**epta, **no**dules, and **f**ibrosis. (SNOF) (Figure 1)
- A ML score (SNOF) was established and tested its association with HVPG, clinically significant portal hypertension (CSPH HVPG ≥10 mmHg) and HVPG ≥12 mmHg.
- Another ML score (SNOF-V) was created for testing association with the presence of varices.

1. Gastroenterology 2020;158:1334–1345

RESULTS

Figure 1. SHG/TPE image showing the AI annotations of septa and nodules, with fibrosis analysed in the portal and peri-portal zones.

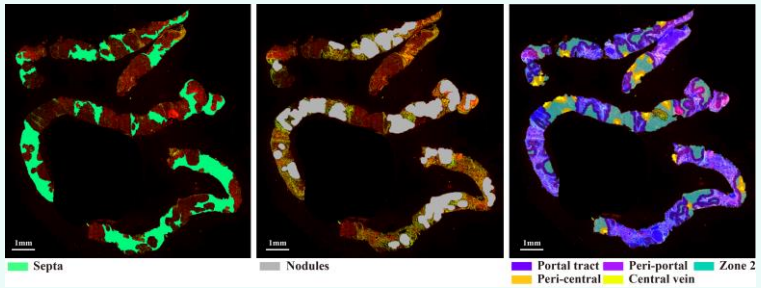

Figure 2. Training and validation plots of SNOF score vs HVPG for baseline (BL) patients. SNOF score is derived from combining the SNOF parameters.

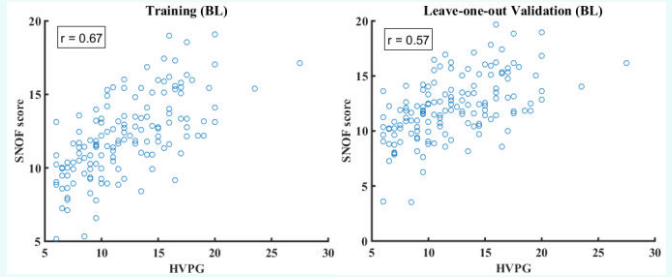

Table 1. Summary of the correlation results among septa, nodules and fibrosis selected parameters when both BL and EOT biopsies were used as training cohort. Correlation of SNOF score built by selecting 15 septa, nodules and fibrosis parameters is also shown.

Parameters	Correlation results (*r* value)					
	Training using BL samples	Leave-one-out validation	Validation on EOT samples	Training using EOT samples	Leave-one-out validation	Validation on BL samples
Septa only	0.55	0.44	0.18	0.56	0.42	0.28
Nodule only	0.52	0.39	0.40	0.53	0.39	035
Fibrosis only	0.57	0.44	0.19	0.62	0.46	0.31
SNOF	0.67	0.57	0.28	0.70	0.61	0.39

- 457 histological parameters (252, 21, and 184 related to septa, nodules, and fibrosis, respectively) were derived.
- BL samples were divided into training/validation and the correlation of each histological parameter with HVPG assessed.
- **Figure 2:** Correlations with HVPG (*p* values <0.05) for the validation cohort are: Septa (r=0.44); Nodule (r= 0.39); Fibrosis (r=0.44).
- In **Table 1**, we show that the combination of **s**epta, **no**dules and **f**ibrosis (SNOF) in an index outperforms using just septa, or nodule, or fibrosis separately.
- The results were similar regardless of whether BL or EOT samples were used as the training cohort.

Table 2. Summary of the performances of SNOF score and SNOF-varices (SNOF-V) scores at predicting HVPG and presence of varices, respectively.

	Baseline					End of treatment				
	AUC	Sensitivity	Specificity	PPV	NPV	AUC	Sensitivity	Specificity	PPV	NPV
SNOF score ≥ 11.78 to predict HVPG ≥ 10 (CSPH)	0.85	73%	86%	91%	62%	0.62	55%	65%	73%	46%
SNOF score ≥ 11.78 to predict HVPG ≥ 12	0.84	83%	74%	75%	81%	0.64	61%	63%	59%	65%
SNOF-V score ≥ 0.57 to predict varices	0.86	77%	86%	85%	78%	0.62	51%	71%	61%	62%
HVPG ≥ 10 to predict varices	0.75	84%	53%	65%	76%	0.72	80%	51%	58%	76%

- SNOF and SNOF-V ML scores are both better than traditional method of using HVPG to predict varices, but only for BL.
- Further analysis with a larger cohort is needed to examine the performances of the ML scores vs traditional HVPG method on EOT cohort.

CONCLUSION

- HVPG was accurately extrapolated from liver histology in patients with NASH cirrhosis by use of a machine learning algorithm, and CSPH and the development of varices were accurately projected.
- Use of ML histological scores may increase accuracy of efficacy endpoints in NASH cirrhosis trials.

DISCLOSURES

For presenting author:
Dr. Mazen Noureddin (MN) has been on the **advisory board** for 89BIO, Gilead, Intercept, Pfizer, Novo Nordisk, EchoSens, Fractyl, Terns, Siemens and Roche diagnostic; MN has **received research support** from Allergan, BMS, Gilead, Galmed, Galectin, Genfit, Conatus, Enanta, Madrigal, Novartis, Pfizer, Shire, Viking and Zydus; MN is a **minor shareholder** or has stocks in Anaetos, Rivus Pharma and Viking.

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