Evaluation of histological differences between cirrhosis due to alcoholic-related liver disease and non-alcoholic steatohepatitis using automated fibrosis phenotyping of liver histology

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Introduction

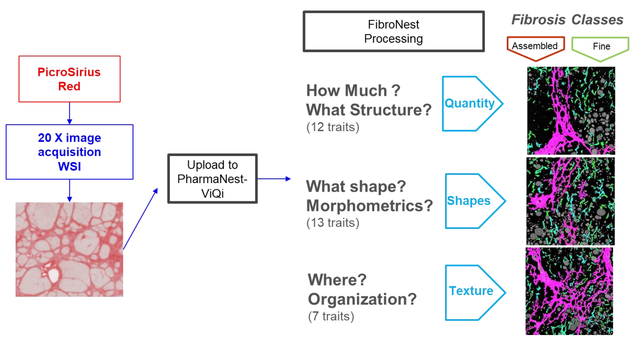
- Liver cirrhosis due to alcoholic-related liver disease (ALD) and non-alcoholic steatohepatitis (NASH) are different diseases with similar histopathology, and histological discrimination can be difficult.
- Although the distinction between ALD and NASH is defined by the amount of alcohol consumed, there is no sufficient consensus because of individual differences in the effects of alcohol.
- Therefore, it is desirable to establish new diagnostic criteria to objectively diagnose ALD and NASH.
- In recent years, digital analysis of pathology has become possible with whole slide imaging systems, which can convert pathology specimens into high-resolution digital images, enabling comprehensive quantitative analysis of pathological parameters using AI.

Aim

This study was to find histological differences between ALD and NASH by analysing more than 300 histological fibrosis phenotypic features.

Method

- Thirty-six patients with cirrhosis due to ALD and 17 patients with cirrhosis due to NASH who underwent liver transplantation at Nagasaki University Hospital between January 2000 and December 2020 were included.
- Tissues of recipient-extracted livers were stained with SiriusRed and imported for digital pathology imaging.
- The FibroNest™ quantitative digital pathology platform (PharmaNest, Princeton, NJ, USA) was used to quantify the histological phenotype of fibrosis, including collagen amount and structure (12 traits), morphometric traits of the collagen fibres (13 traits), and architecture of fibrosis (7 traits).
- Each traits considers mean, variance, skewness, kurtosis and progression, for a total of over 300 parameters to compare differences in histological features between ASH and NASH.



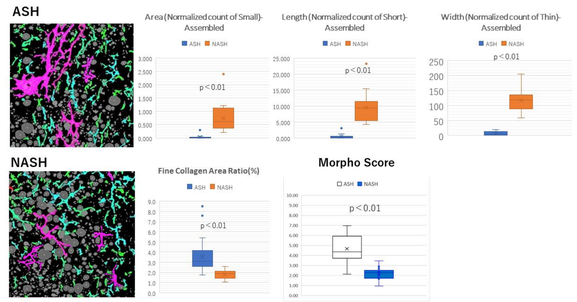
Results

Table 1

Characteristic of 53 patients

	Total(n=53)	ASH (n=36)	NASH (n=17)	p-value
Age (years)	60.0 (53-64)	58.5 (52-63)	63.0 (57-65)	NS
Sex (male/female)	38:15	31:5	7:10	0.002
BMI (Kg/m^2)	24.8 (21.8-27.3)	23.7 (21.6-26.4)	26.4 (23.7-28.2)	NS
MELD score	17 (13-23)	17 (11-22)	19 (14-25)	NS
Plt (10^4/μl)	5.5 (4.5-8.7)	5.9 (4.2-8.6)	5.5 (4.9-8.8)	NS
PT-INR	1.60 (1.38-1.83)	1.56 (1.35-1.86)	1.66 (1.38-1.78)	NS
ALB (g/dl)	2.6 (2.4-2.9)	2.5 (2.4-2.8)	2.6 (2.4-2.9)	NS
T-Bil (mg/dl)	3.1 (1.9-8.1)	2.8 (1.7-7.5)	3.5 (2.6-8.2)	NS
Fib-4 index	7.53 (4.8-10.6)	7.41 (4.7-10.7)	8.12 (5.1-11.4)	NS
Hyarulonic acid	972 (469-3195)	1171 (484-4185)	937 (427-2015)	NS

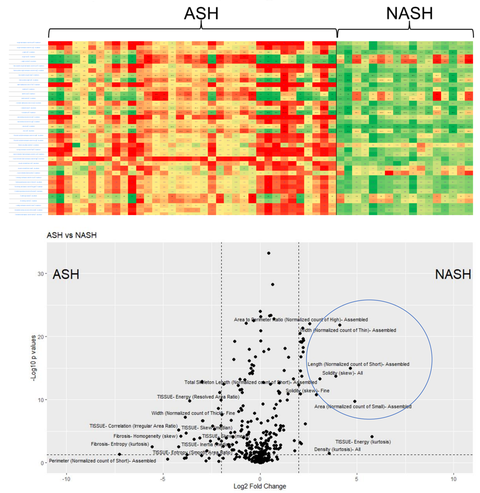
Figure 2



The NASH group was characterized by assembled collagen, which defined a complex skeleton with a high number of nodes and branches, were short in length, thin, and small in area.
On the other hand, the ALD group had significantly more fine collagen than the NASH group.

Figure 1

Comparison **of morphological traits of ASH and NASH**

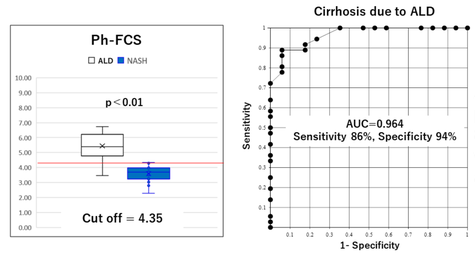


There were no significant differences in collagen amount, structure, and architecture of fibrosis between ASH and NASH.

However, morphometric traits of the collagen fibres were significantly different between the two groups as shown in the heat map

The volcano plot shows that there are differences in traits associated with assemble collagen in the NASH group compared to the ASH group.

Figure 3



A diagnosis of ALD/ NASH was possible with a sensitivity of 86% and specificity of 94% when the cut-off value was set at 4.35

Phenotypic Fibrosis Composite score (Ph-FCS) created from 350 quantitative fibrosis traits normalized to their maximum value in the group and then averaged.

Conclusions

The analysis of fibrosis patterns by digital pathology suggested the possibility of discriminating the histological diagnosis of ALD/ NASH by differences in fibrosis morphology.

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