THU-428

Digital pathology with artificial intelligence analyses provides deeper insights into lifestyle intervention-induced fibrosis regression in NASH

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Background and Aims: Lifestyle intervention is the basic treatment for non-alcoholic steatohepatitis (NASH) and liver fibrosis is a crucial determinant of clinical outcome in this condition. The second harmonic generation/two-photon excitation fluorescence (SHG/TPEF) microscopy with artificial intelligence analyses can provide automated quantitative assessment of fibrosis features on a continuous scale, called qFibrosis. We used this approach to gain insight into the impact of lifestyle intervention intensity on fibrosis in NASH.
Method: Unstained sections from 72 liver biopsies (paired: baseline and end-of-treatment) from 36 NASH patients who received routine lifestyle intervention (RLI, n = 24) or strengthen lifestyle intervention (SLI, n =12) were examined. Fibrosis regression was determined by pathological reading. Liver fibrosis (qFibrosis) were quantified by SHG/TPEF microscopy. Collagen parameters were quantified from the five regions, including portal tract (PT), peri-PT, Zone 2, central vein (CV) and peri-CV, which were identified from the SHG/TPEF images.
Results: 21% (5/24) and 50% (6/12) of patients had fibrosis regression for RLI group and SLI group, respectively. 50% of patients had fibrosis no change for both RLI and SLI groups. Numerical analysis showed that fibrosis progression tended to no change or regression in NASH patients after lifestyle interventions, and this phenomenon was more pronounced in the SLI group. Among the patients with fibrosis regression, compared with the RLI group, the fibrosis index of SLI group was reduced more ($p<0.001$) in the PT, peri-CV and CV regions, but increased more ($p<0.001$) in zone 2 region. In patients with no change in the fibrosis outcome of conventional pathology, we found a more significant regression in zone 2 region in the SLI group than the RLI group.
Conclusion: With enhanced lifestyle intervention, we can see a more pronounced regression of fibrosis, mainly in the portal and central vein segments for the regression patients. Digital pathology provides new insights into lifestyle intervention-induced fibrosis regression, which are not captured by current staging systems.

Table: Average relative difference of parameters in different regions between RLI group and SLI group in regression patients and no change patients.

Region	Regression patients			No change patients		
	RLI (n=5)	SLI (n=6)	p value	RLI (n=12)	SLI (n=6)	p value
PT	73%	-32%	<0.001	30%	31%	0.452
Peri-PT	13%	-4%	0.053	-31%	1%	<0.001
Zone 2	-17%	18%	<0.001	-14%	-30%	<0.001
Peri-CV	97%	-81%	<0.001	65%	99%	<0.001
CV	84%	-78%	<0.001	92%	79%	0.063

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1 Introduction

- Lifestyle intervention is the basic treatment for non-alcoholic steatohepatitis (NASH) and liver fibrosis is a crucial determinant of clinical outcome in this condition.
- The second harmonic generation/two-photon excitation fluorescence (SHG/TPEF) microscopy with artificial intelligence analyses can provide automated quantitative assessment of fibrosis features on a continuous scale, called **qFibrosis**.

2 Aim

- We aimed to gain insight into the impact of lifestyle intervention intensity on fibrosis in NASH.

3 Method

1. Grouping: divided into the strengthen lifestyle intervention (SLI) group and the routine lifestyle intervention (RLI) group according to the intensity of the lifestyle intervention.
   - **SLI group**: stick to a limited daily calorie intake according to the personalized diet plan developed by the dietitian; adhere to some degree of aerobic exercise and resistance exercise.
   - **RLI group**: self-regulate diet and physical exercise.

2. Technology and equipment:
   - **SHG/TPEF microscopy**: a fully automated, stain-free multiphoton fluorescence imaging microscope.
   - **qFibrosis**: the overall output from assessment of fibrosis in the liver specimen comprising the quantitative readouts from 140 fibrosis parameters on a linear scale.

4 Results

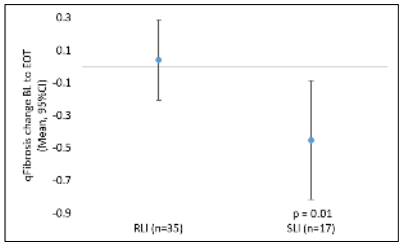

Figure 1. Changes of qFibrosis from baseline (BL) to the end of treatment (EOT) in RLI group and SLI group.

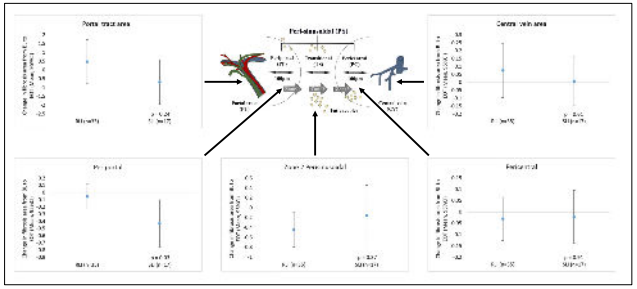

Figure 2. Percentage change of zonal fibrosis quantitation from BL to EOT in each region.

- With the increase of the intensity of life intervention, qFibrosis showed a marked decline.
- It was observed that the fibrosis area in the periportal area in the SLI group was significantly decreased compared with the RLI group.
- P/N/R analysis revealed that with the increase of the intensity of life intervention, the progression of fibrosis was prominently relieved.
- Among the patients with fibrosis regression, significant fibrosis regression was observed in the portal region, peri-portal region, central vein region and peri-central vein region in the SLI group. In patients with no change in fibrosis, the SLI group showed significant regression of fibrosis in zone 2.

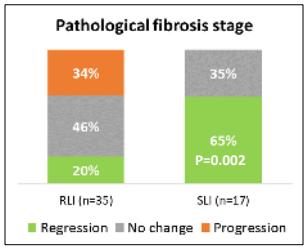

Figure 3. Progression/ No change/ Regression (P/N/R) analysis of fibrosis changes from BL to EOT, based on the NASH CRN score.

Region	Regression patients			No change patients		
	RLI (n=7)	SLI (n=11)	p value	RLI (n=16)	SLI (n=6)	p value
PT	39%	-60%	<0.001	24%	27%	0.927
Peri-PT	-10%	-26%	<0.001	-27%	1%	<0.001
Zone 2	-18%	12%	<0.001	-10%	-29%	<0.001
Peri-CV	93%	-20%	<0.001	22%	100%	<0.001
CV	100%	-28%	<0.001	63%	85%	0.043

Table 1. Average relative difference of fibrosis parameters in different regions.

5 Conclusions

- With enhanced lifestyle intervention, we can see a more pronounced regression of fibrosis.
- Digital pathology provides new insights into lifestyle intervention-induced fibrosis regression, which are not captured by current staging systems.

6 Acknowledgements

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7 References

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