

# Differences in metabolites and physiological maker between hepatic venous pressure gradients by portal vein blood in patients with liver fibrosis

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Sang Youn Lee<sup>1</sup>, Su Been Lee<sup>1</sup>, Kyeong Jin Lee<sup>1</sup>, Jung A Eom<sup>1</sup>, Sung Min Won<sup>1</sup>, Dong joon Kim<sup>1</sup>, Ki Tae Suk<sup>1</sup>

<sup>1</sup>Institute for Liver and Digestive Diseases, Hallym University College of Medicine, Chuncheon, Korea.

## BACKGROUND

Liver fibrosis interferes with normal function by altering the structure of a particular organ and is one of the main causes of death. Liver cirrhosis (LC) is defined as an advanced stage of liver fibrosis with hepatic vasculature and structural distortion. The development of portal hypertension is characteristic of LC. We investigate the difference in metabolites in portal vein blood according to the degree of hepatic venous pressure gradient (HVPG) in patients with hepatic fibrosis.

## METHODS

We used humanely collected portal vein blood (PVB). We mixed PVB with Acetonitrile:3'-distilledwater=1:1 (v/v) and centrifuged at 13200 rpm and 4°C for 5 minutes after vortex for 1 min and sonicate for 5 min under ice. After transferring the supernatant to a new tube, Acetonitrile:Methanol=1:3 (v/v) was added and then proceeded as described above. The supernatant was transferred to a new tube and concentrated with a speed vacuum concentrator. The HPLC conditions used were as follows: column temperature was set at 30 °C, injection volume was 10 µL, mobile phase A was water with 0.1% formic acid and mobile phase B was 5 acetonitrile.

## RESULTS

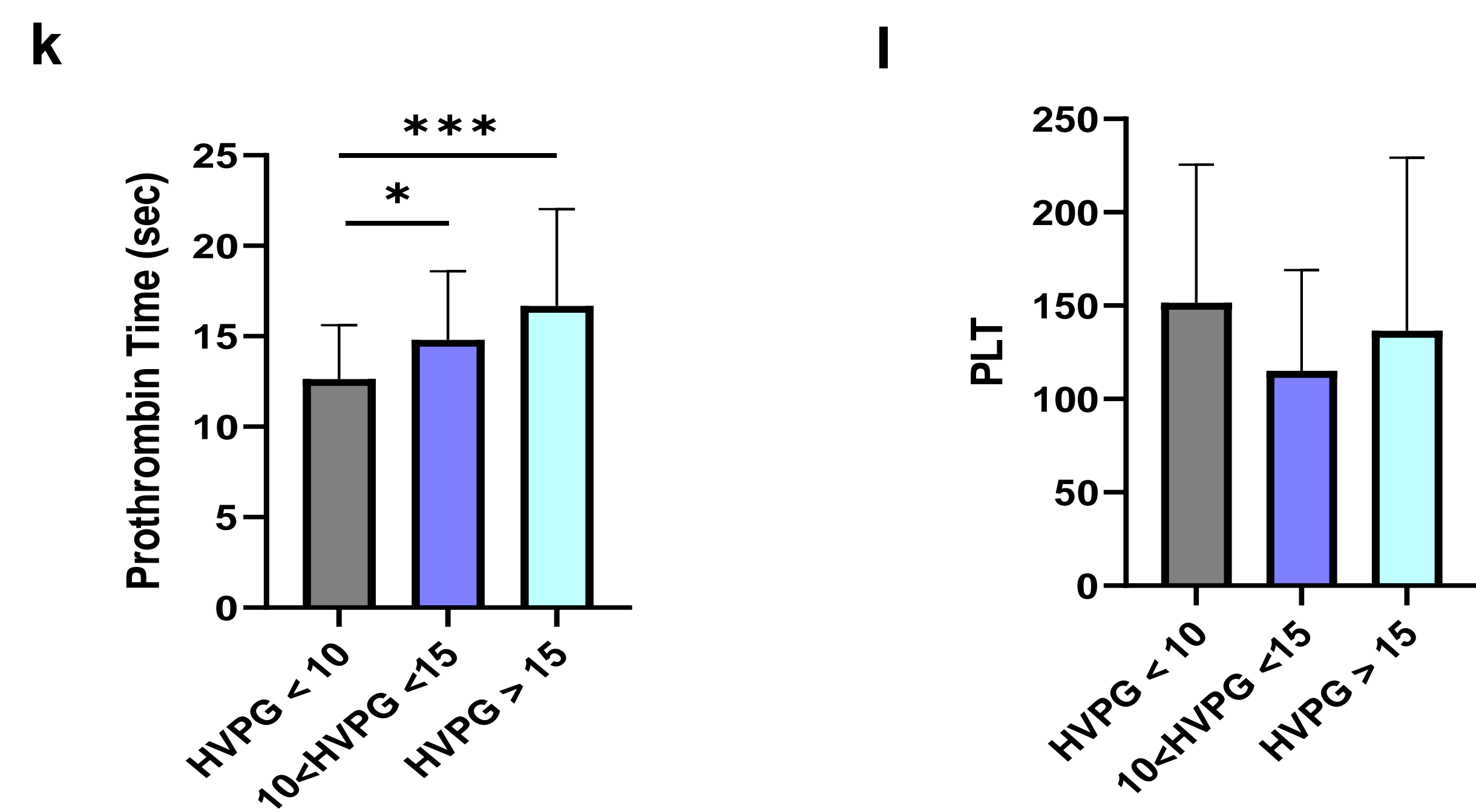
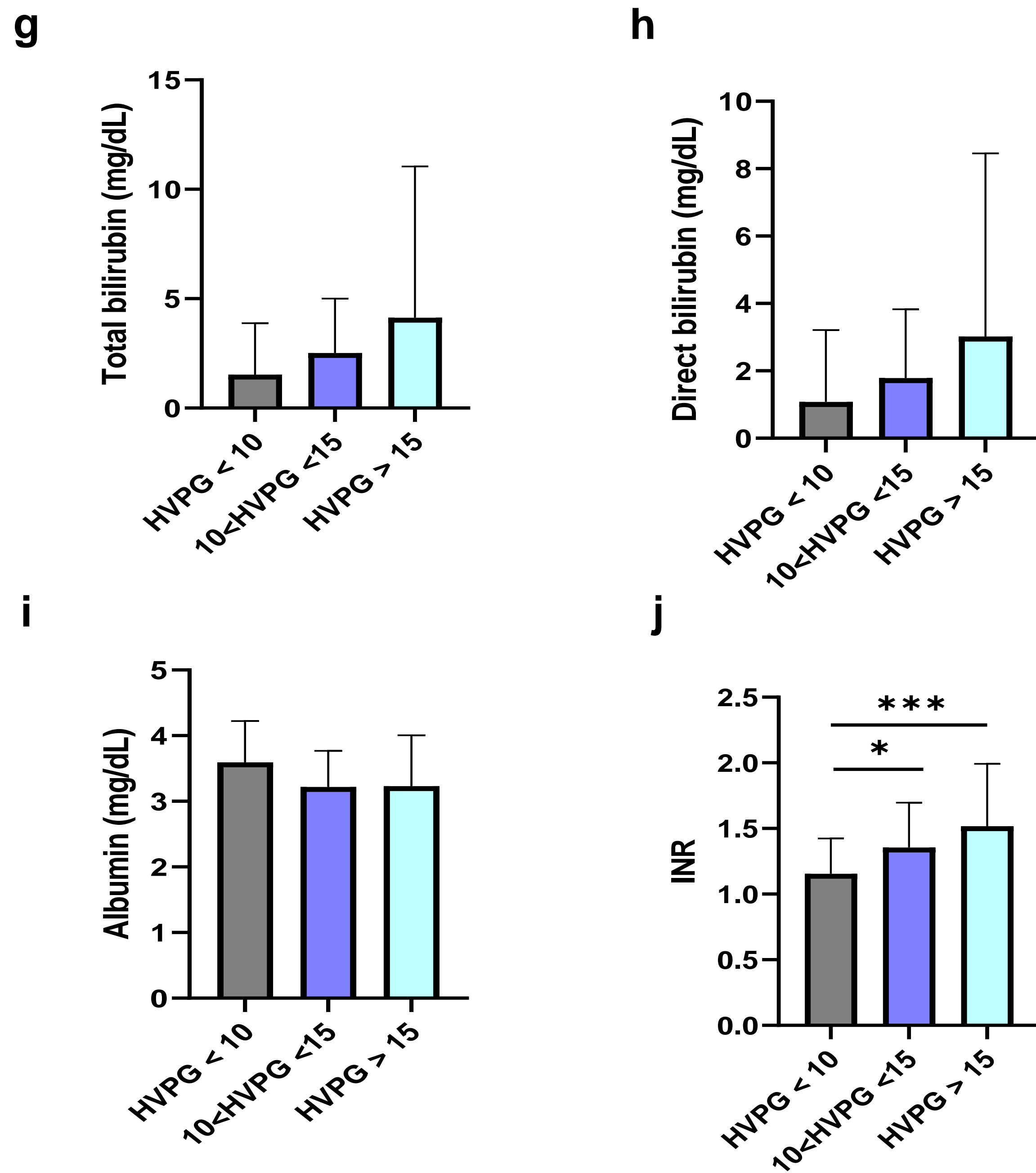
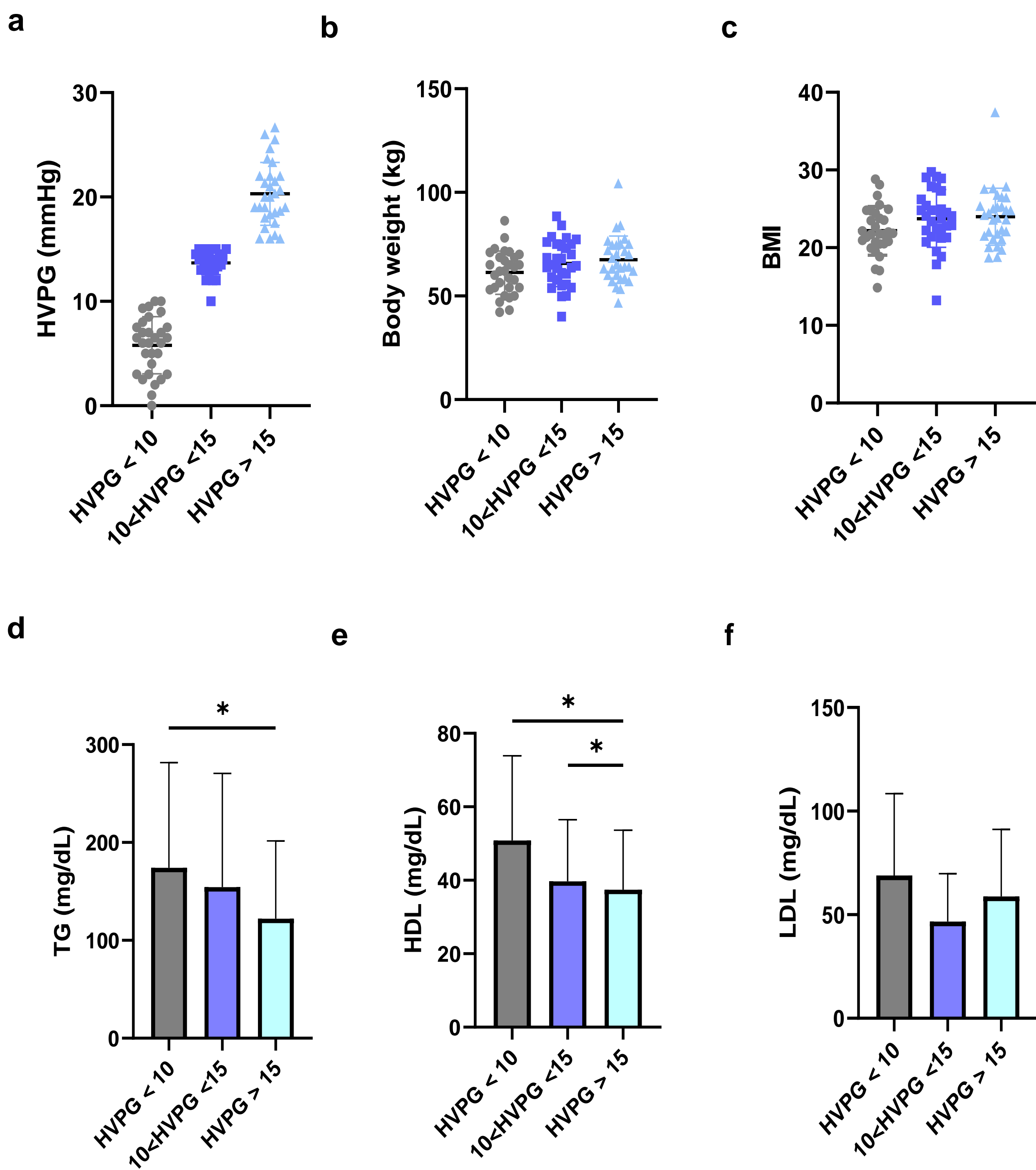
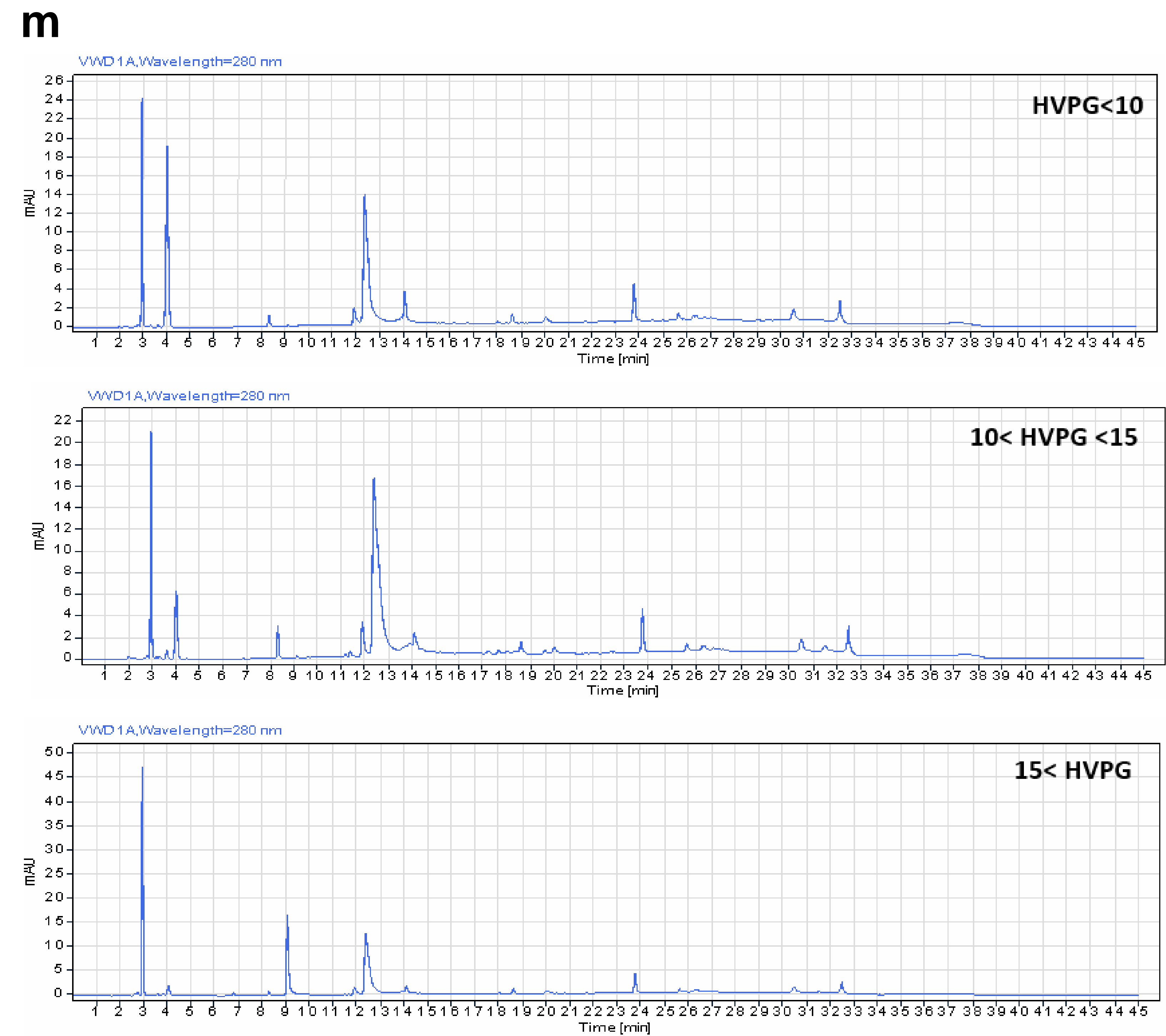


Figure: Basic and biochemical indicators based on HVPG values. (a) HVPG metrics for each group, (b) & (c) body weight and BMI index for each group, (d) & (e) & (f) blood biochemical index for each group, 10 < HVPG group significantly decreased in HDL index compared with HVPG < 10, (g) & (h) bilirubin index for each group, (i) albumin index for each group, (j) 10 < HVPG group significantly increased in INR index compared with HVPG < 10, (k) 10 < HVPG group significantly increased in Prothrombin time index compared with HVPG < 10, (l) PLT index for each group, (m) the HPLC chromatogram for each group.



We measured the biochemical indicators HVPG, ALT, AST and Albumin using humanely collected PVB. The group consisted of three stages according to the degree of HVPG. The average HVPG of each group was  $6\pm2.3$ ,  $14.1\pm0.4$ , and  $22.2\pm4.2$ , showing differences between groups. The intergroup AST indices were  $57\pm14.5$ ,  $74\pm37.6$ , and  $103\pm48.7$ , indicating a proportional increase with increasing HVPG values. However, ALT and Albumin indices did not show differences between groups. In addition, meaningful results can be found in HDL, INR, and Prothrombin time indicators when checking blood biochemical indicators. PVB was sampled in each group and metabolite was analyzed by HPLC to confirm differences between groups. At the peak of retention time 4, 14 minutes, it can be seen that the area value is 139.4, 45.4, 16.2 mAU and 21.2, 9.2, 7.1 mAU and low from the group with high HVPG. On the other hand, at the peak of Retention time 9 minutes, it can be seen that the group with high HVPG has a large area value of 0.3, 0.8, and 107.6 mAU.

## CONCLUSION

We investigated differences in biochemical indices and metabolites in PVB in patients with liver fibrosis according to the degree of HVPG. Differences in biochemical indices according to the stage of HVPG were confirmed. In addition, metabolites were confirmed through HPLC, and differences in patterns depending on the stage were confirmed. This suggests that hepatic fibrosis patients can be a maker of severity without measuring HVPG.