Gut immunity and integrity markers in acute on chronic liver failure

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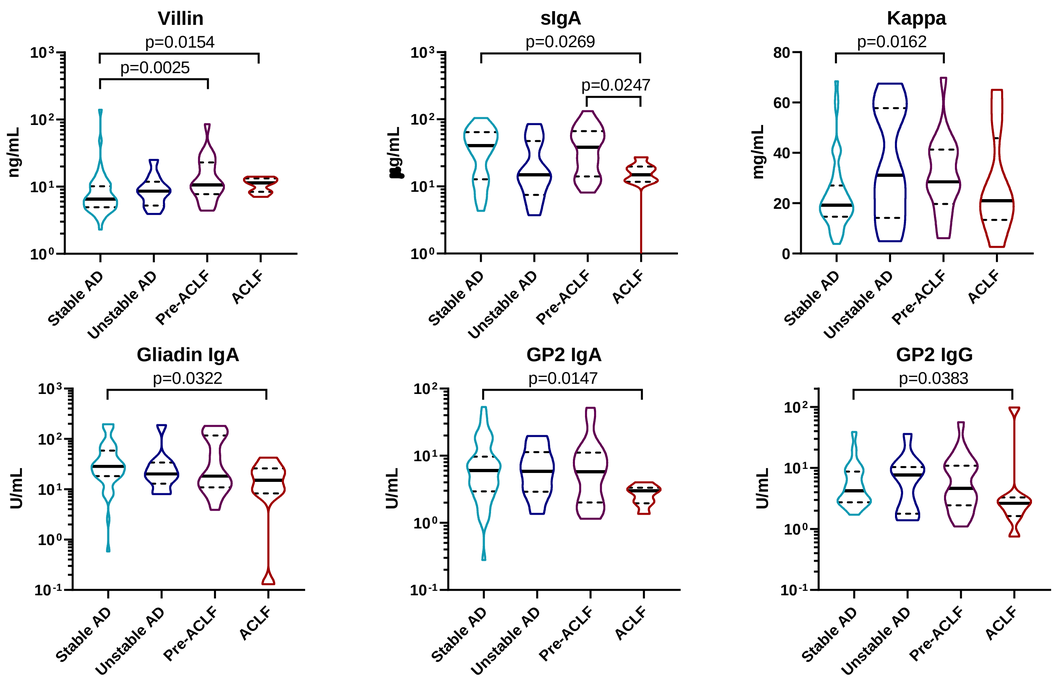
INTRODUCTION

- Cirrhosis → alterations in the gut microbiota, small intestinal bacterial overgrowth, disturbance of mucosal immunity and intestinal barrier integrity → sustained leakage of bacterial antigens from the gut lumen to the portal circulation (i.e., bacterial translocation, BT) → activation of proinflammatory signaling cascade → enhanced tissue damage of the liver → acceleration of chronic liver disease progression.
- Plasma cells and the antibodies they produce play a pivotal role in intestinal immunity.
- In the hepatobiliary system and gut mucosa, the vast majority of plasma cells engages towards IgA production → IgA is responsible for protection and tolerance against the intestinal flora of the gut.
- BT continuously induces B-cell proliferation and differentiation leading to pathologically enhanced production of IgA type antibodies and ultimately the formation of various autoreactive IgA subspecies in cirrhotic patients.
- Therefore, we hypothesized that serologic markers of BT, gut integrity and immunity can reliably reflect pathological processes in the gut mucosa.

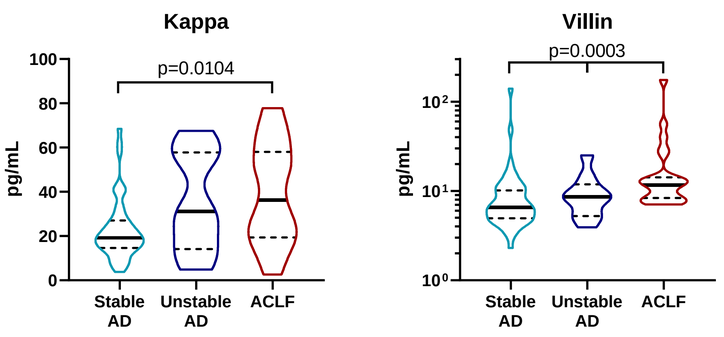
METHODS AND RESULTS

- ELISA and indirect immunofluorescent techniques were applied to determine levels and presence of 20 serological markers of the gut barrier function
- in 91 cirrhotic patients with acute decompensation (AD)
  - » 52 stable AD, 10 unstable AD, 21 Pre-ACLF and 8 ACLF patients
- at baseline and at time of readmission due to ACLF

Markers showing significant differences among groups



Differences among groups using all ACLF events (primary & secondary*)

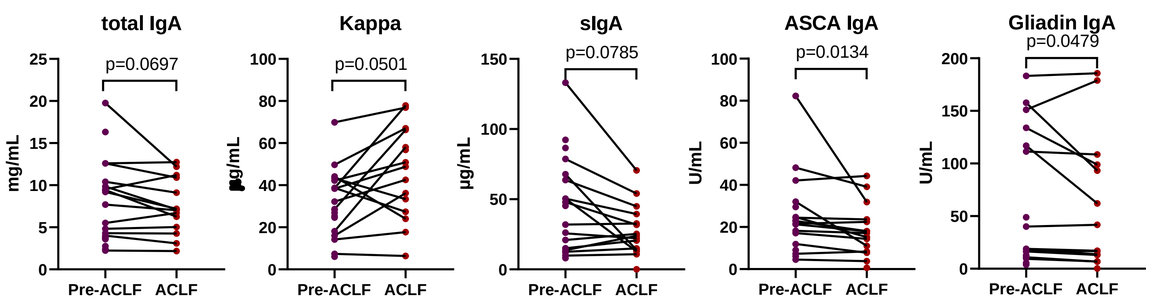


n=52
n=10
n=23

* Primary ACLF: patients with ACLF at inclusion

Secondary ACLF: ACLF visit of patients with pre-ACLF at admission

Intraindividual differences at the time of pre-ACLF and ACLF

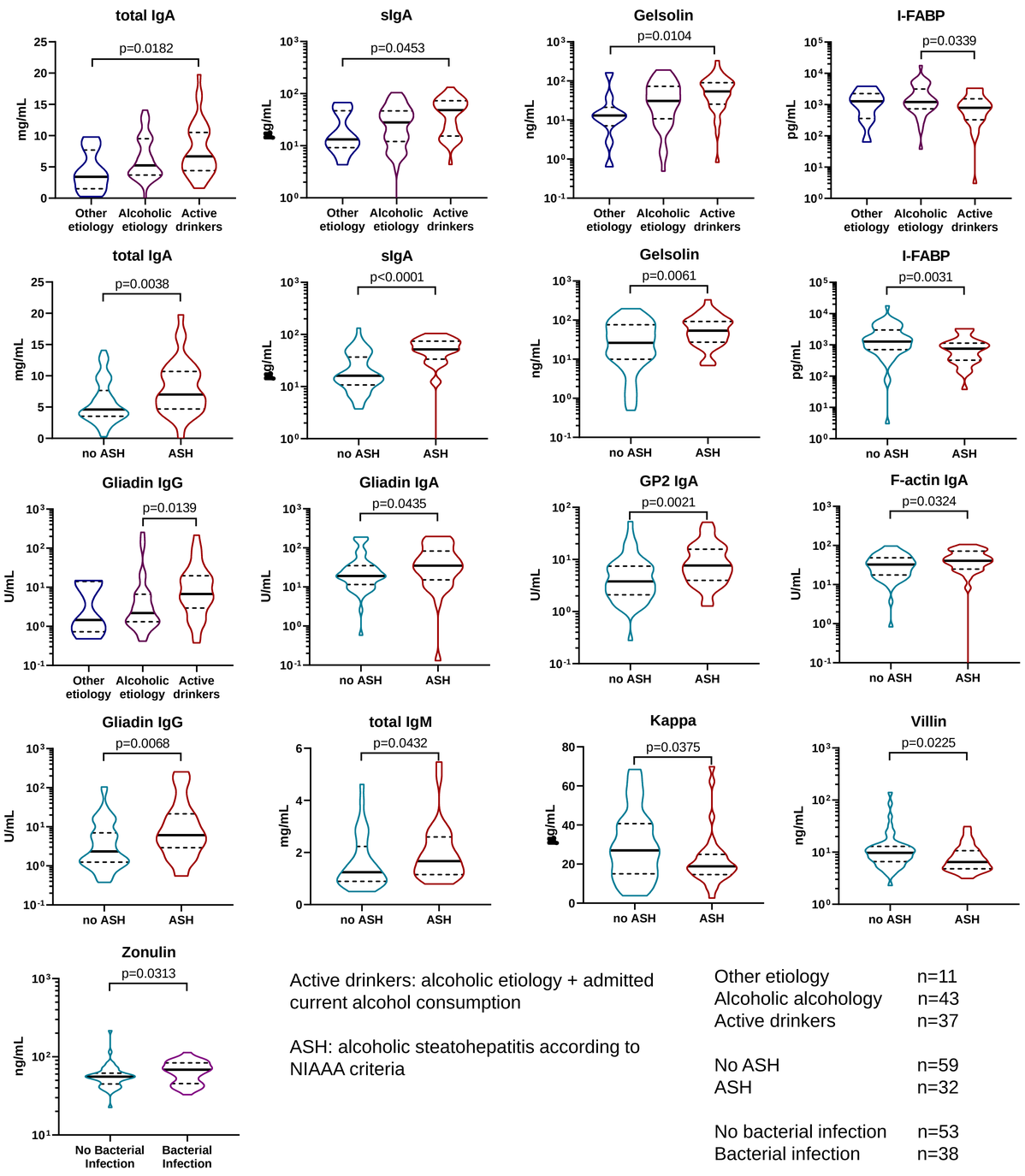


n=21 n=15

#Due to low number of cases, close-to-significant values are also shown

RESULTS (continuation)

Differences according to precipitating factors (alcohol usage & bacterial infection)



Active drinkers: alcoholic etiology + admitted current alcohol consumption

ASH: alcoholic steatohepatitis according to NIAAA criteria

Other etiology	n=11
Alcoholic alcohology	n=43
Active drinkers	n=37
No ASH	n=59
ASH	n=32
No bacterial infection	n=53
Bacterial infection	n=38

SUMMARY AND CONCLUSIONS

- Cirrhotic patients with AD were categorized into groups according to outcomes
- The individual groups did not have enough patients for profound statistical analyses, sub-group assessments and detection of significant differences in most cases
- Some differences were detected among groups, mostly between stable AD and ACLF patients
- Boosting the number of ACLF samples with samples obtained at readmission due to ACLF of originally pre-ACLF patients did not increase the identification of marker candidates, which might indicate that the two ACLF groups (primary & secunder) are not homogenous
- ASCA IgA and Gliadin IgA are significantly decreased at time of ACLF events compared to pre-ACLF events of the same patients
- Alcohol consumption seems to influence the markers of the gut immunity and barrier integrity much more widely than the outcome groups.
- Villin, sIgA and Gliadin IgA seem worthwhile to be measured in the entire PREDICT cohort.

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