Spleen size does not correlate with histological stage of disease in NAFLD

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INTRODUCTION

In the context of liver disease, splenomegaly is commonly associated with portal hypertension1, driven by multiple factors including portal congestion, tissue hyperplasia and fibrosis.

However, increased spleen longitudinal diameter has been reported in association with the metabolic syndrome and obesity2,3, both key drivers of non-alcoholic fatty liver disease (NAFLD).

Through clinical experience, we noted an increasing number of patients undergoing extensive investigation for splenomegaly in the context of NAFLD.

We hypothesised that specifically in NAFLD, splenomegaly was not associated with the severity of underlying liver disease, and was determined by alternative factors.

AIM

In this study, we sought to test the correlation between histological stage of liver disease and longitudinal spleen size in a large group of subjects with biopsy-proven NAFLD.

METHOD

We undertook a retrospective analysis of all patients undergoing a liver biopsy for NAFLD staging between January 2015 and December 2019 and those who had a sonographic measurement of longitudinal spleen diameter within one year of their biopsy.

Liver biopsies were scored by a specialist liver histopathologist using the Clinical Research Network (CRN) scoring system for steatosis (S0-S3), ballooning (B0-B2), inflammation (I0-I4) and fibrosis (F1-F4). Height and weight were measured using standard methods.

Fasting Lipid profile and glycated haemoglobin (HbA1c) were measured using standard methods.

Data was analyzed using Fisher's exact test (categorical data), simple linear regression (continuous data) and multiple linear regression using GraphPad Prism v8.

RESULTS

We identified 275 patients with a diagnosis of NAFLD who had paired biopsy and spleen size measurement. Fibrosis scores were distributed between F0 and F4. Splenomegaly was present in 44.7% of the cohort. There was no correlation between spleen size and histological stage of liver disease.

There was no difference between individual and sum components of the NAFLD activity score and the presence of splenomegaly, defined as a spleen size greater than 12 cm.

Platelet count on the other hand showed a strong inverse correlation with progressive stages of liver disease.

Spleen size correlated negatively with age, and positively with body weight, height and body mass index (BMI).

Interestingly, body weight showed the strongest correlation with spleen size.

Histological, clinical and metabolic features of patients in the cohort. The association between splenomegaly and biopsy features was tested using a Chi squared test. The association between spleen size and anthropometric and metabolic parameters was tested using simple linear regression. Associated variables were tested in a multiple regression analysis. Age, body weight and HDL cholesterol were the main determinants of spleen size.

<table>
<thead>
<tr>
<th>BIOPSY</th>
<th>Univariate Analysis</th>
<th>Multivariate analysis</th>
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<tbody>
<tr>
<td>F0-F4</td>
<td>OR 0.63 p 0.0003</td>
<td>OR 0.61 p 0.0003</td>
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<tr>
<td>S0-S3</td>
<td>OR 0.30 p 0.0001</td>
<td>OR 0.61 p 0.0003</td>
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<tr>
<td>B0-B2</td>
<td>OR 0.50 p 0.0002</td>
<td>OR 0.61 p 0.0003</td>
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<tr>
<td>I0-I4</td>
<td>OR 0.30 p 0.0001</td>
<td>OR 0.61 p 0.0003</td>
</tr>
<tr>
<td>F1-F4</td>
<td>OR 0.30 p 0.0001</td>
<td>OR 0.61 p 0.0003</td>
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ANTHROPOMETRY

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Mean ± SD</th>
<th>R²</th>
<th>t statistic</th>
<th>p</th>
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<tbody>
<tr>
<td>56.0 ± 10.3</td>
<td>0.05</td>
<td>1.98</td>
<td>0.05*</td>
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CONCLUSIONS (1)

In this retrospective cohort with biopsy-proven and staged NAFLD, spleen size was not associated with histological grade of liver disease.

- Spleen size should not be used as an indicator of the severity of parenchymal disease in NAFLD.
- Further studies are required to formally test whether splenomegaly is independently associated with portal hypertension in NAFLD.
- Spleen size alone is unlikely to be a good indicator of disease progression in NAFLD. We propose that alternative parameters should be used to monitor disease progression to portal hypertension, including:
  - platelet count,
  - measures of liver and spleen stiffness
  - radiological assessment of blood flow in the portal, splanchic and collateral circulations.

CONCLUSIONS (2)

Body weight, age and HDL are the strongest predictors of spleen size in this patient group.

We propose that:
- The spleen may be a site for visceral deposition of ectopic fat.
- The spleen may sequester HDL in lymph.

Further studies are required to test for associations between NAFLD and the prevalence of major cardiovascular events in NAFLD.

REFERENCES