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THE SIGNIFICANCE OF FAT DROPLET SIZE AND THE PROGNOSTIC VALUE OF HYALURONIC ACID IN NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD): A BIOPSY BASED ANALYSIS

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Introduction There are little data regarding the significance of fat droplet size or degree of hepatic steatosis in NAFLD. Microvesicular steatosis is thought to be rare in NAFLD. The aims of this study were to assess the prevalence of microvesicular steatosis and determine whether droplet size and amount of steatosis are clinically relevant. A further aim was to determine if hyaluronic acid (HA), a non-invasive

marker of fibrosis, was helpful in discriminating fibrosis in NAFLD.

Methods A database of liver biopsies performed between 1998 and 2009 at the Royal Infirmary of Edinburgh was interrogated and patients with NAFLD identified. Cases with co-existent liver disease or medication that would result in hepatic steatosis were excluded. Pathology and case notes were then reviewed.

Results *Demographics:* 59 patients were included: 56% male; mean age 47 years. 39% had insulin resistance (IR) and 20% diabetes. On biopsy, 9 (15%) patients had microvesicular, 30 (51%) macrovesicular and 18 (30%) mixed steatosis. *Steatosis:* Microvesicular steatosis was associated with a reduced incidence of IR and diabetes ($p=0.016$). There was a significant difference in GGT between micro and macrovesicular steatosis (278 vs 107 U/l; $p=0.05$). However, there was no correlation between droplet size and disease activity (either by ALT or NAFLD activity score). There was a trend to a correlation between microvesicular droplets and less fibrosis ($p=0.066$) and lower amounts of total steatosis ($p=0.053$). Total amount of steatosis on biopsy did not show any further significant correlations. *Fibrosis Scores:* There was a significant correlation between HA and fibrosis ($p=0.003$). Post-test analysis demonstrated a significant trend between increasing fibrosis scores and increasing HA levels ($p=0.001$). AUC for fibrosis grade 3 or 4 was 0.89 (95% CI >0.75 to 1.03). A ROC curve indicated as a cut off value of 85 ng/ml would indicate severe fibrosis (sensitivity of 86%; specificity 89%).

Conclusion Microvesicular steatosis represented 15% of cases and was associated with less insulin resistance and a higher GGT. It is possible that different stages of NAFLD severity are associated with different size of fat droplet but not significant change in the quantity of fat in the liver. HA is sensitive at assessing fibrosis of NAFLD irrespective of inflammation or amount of fat on biopsy.

Competing interests None.

Keywords biopsy, fatty liver, hyaluronic acid, steatosis.