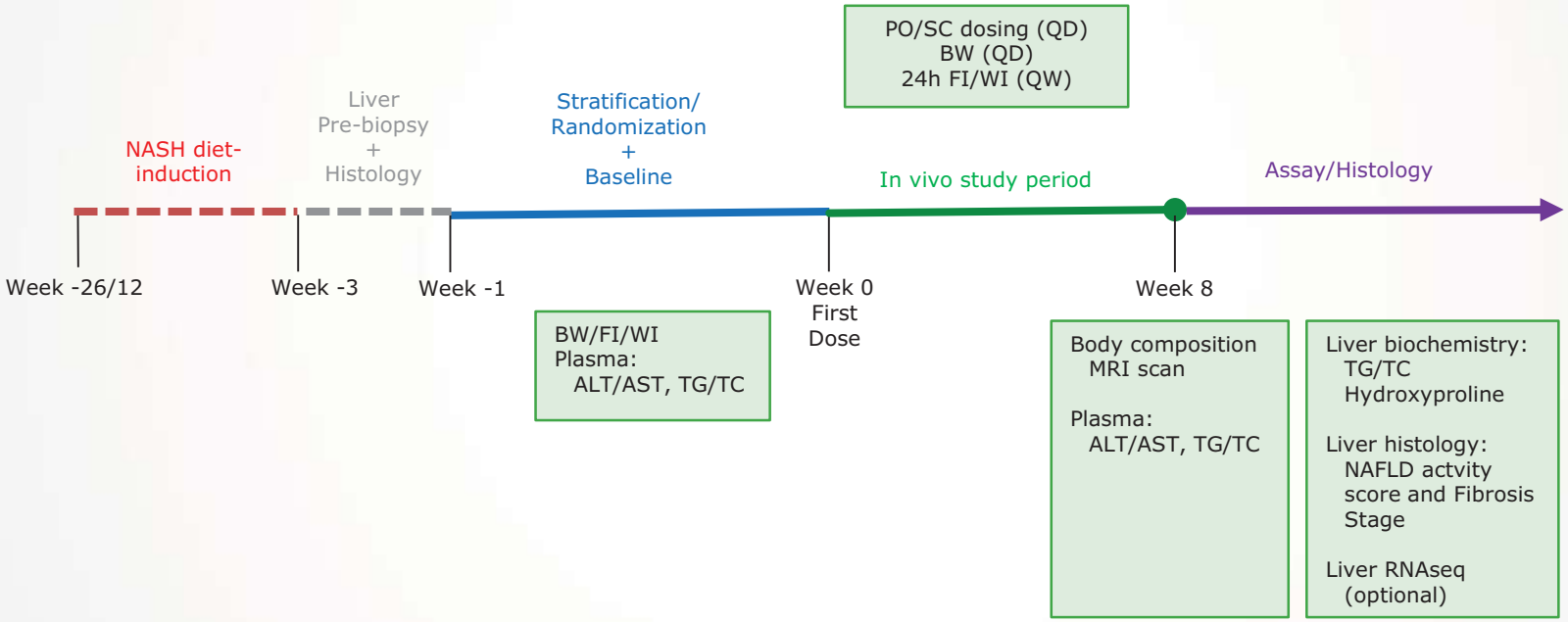
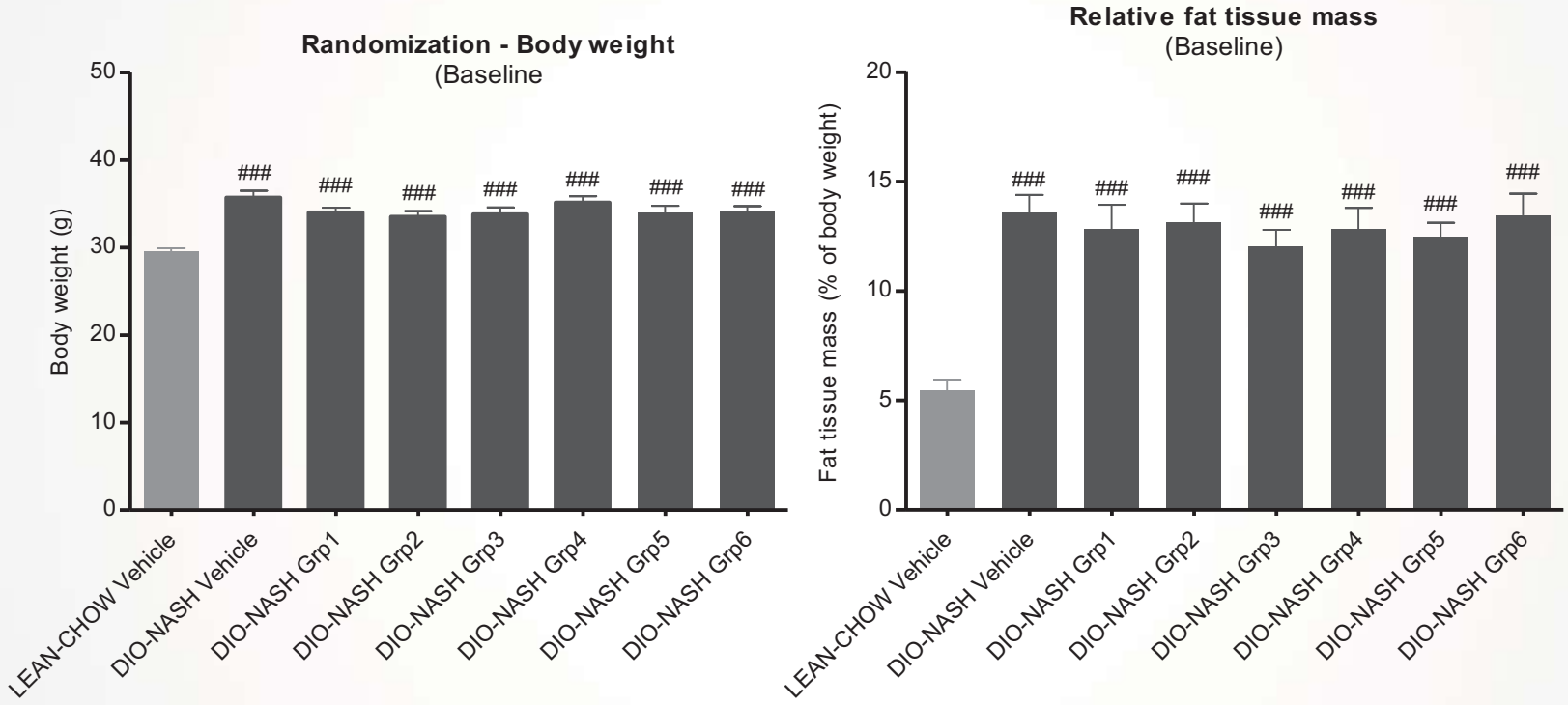
GUBRA DIO-NASH model

The Gubra DIO NAFLD/NASH model reflect characteristics of fatty liver disease and NASH

Gubra NASH study design

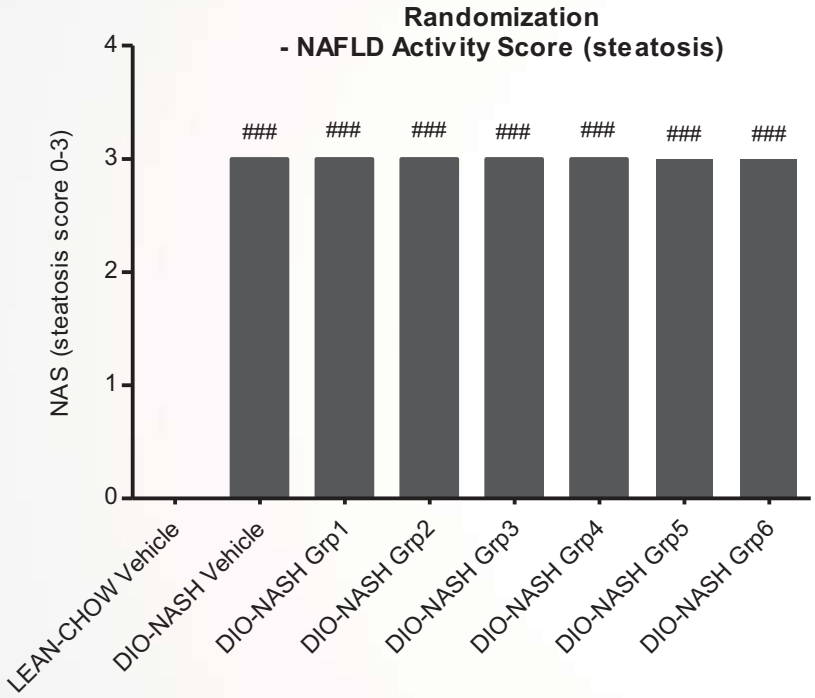


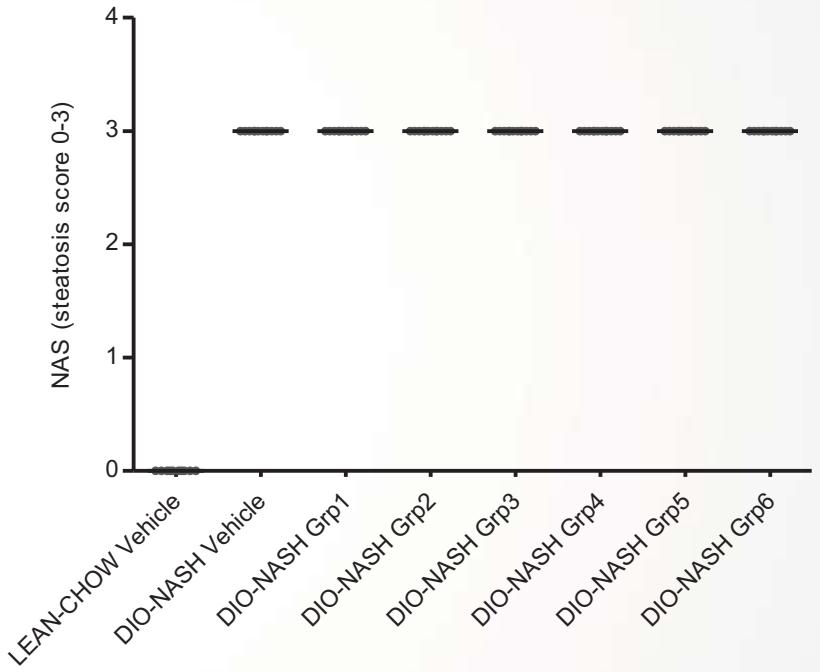
Randomization – Body weight and fat mass



Increased body weight and adiposity (DIO)

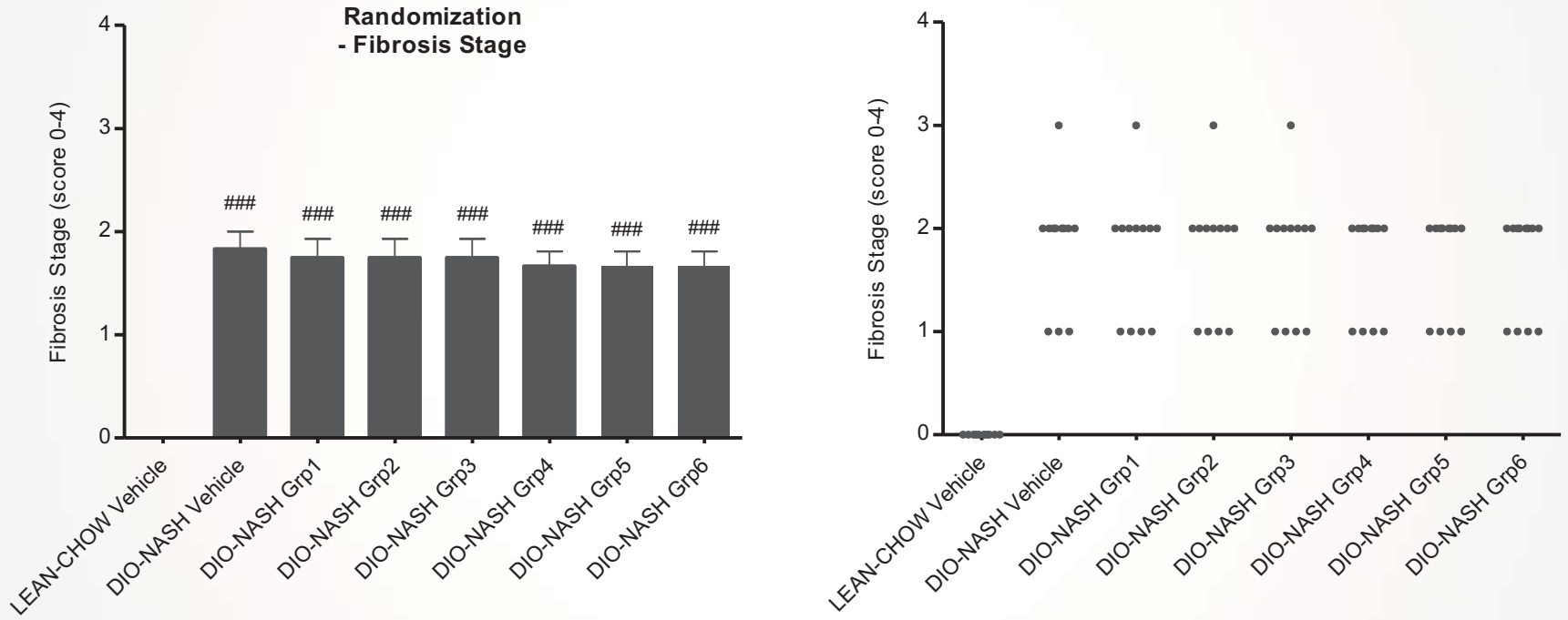
Randomization – Liver steatosis





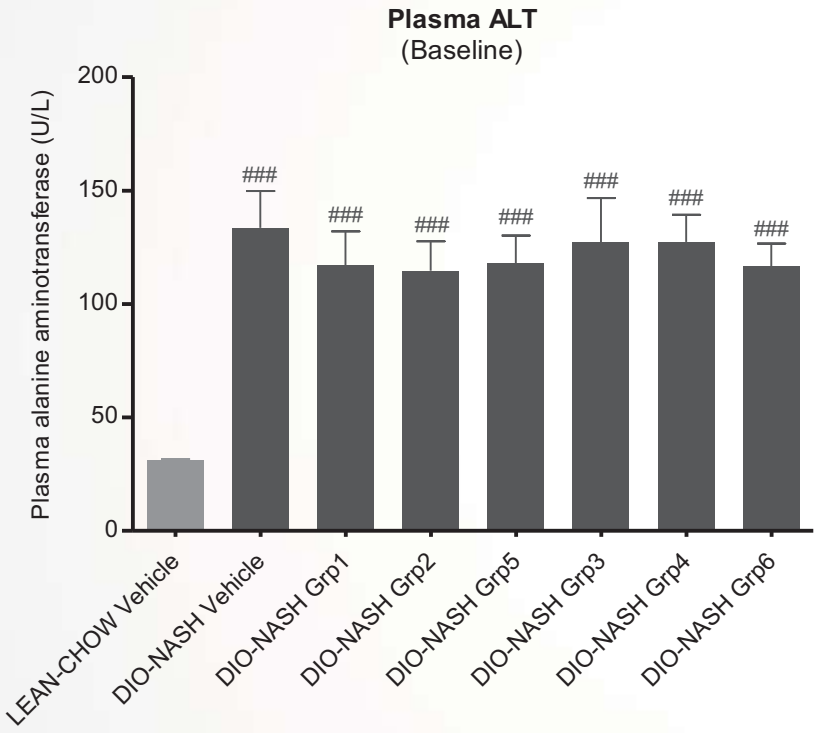
Steatosis score of 2-3 to be enrolled into study

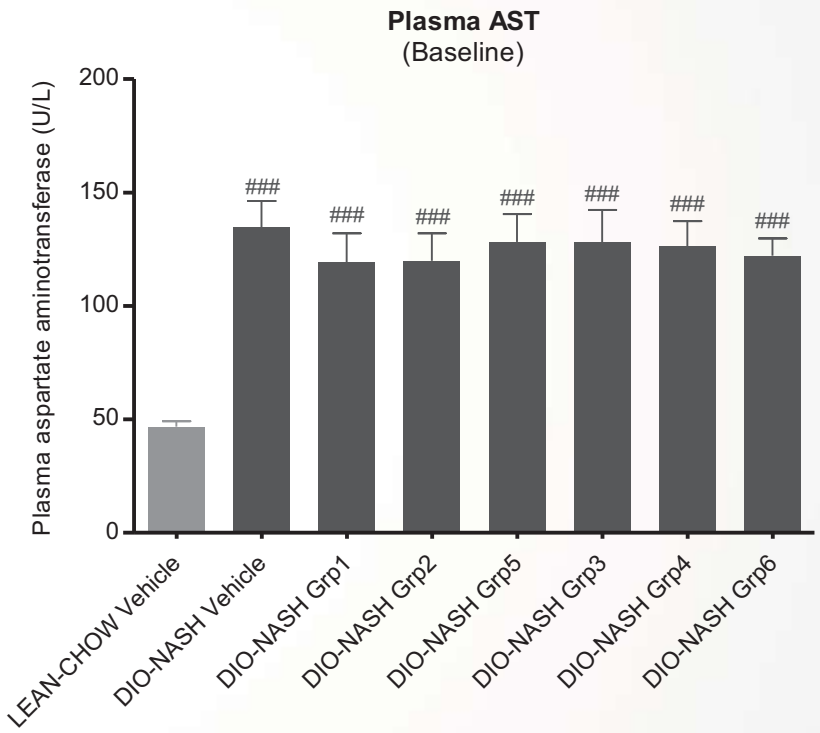
Randomization – Liver fibrosis



F1-F3 to be enrolled into study

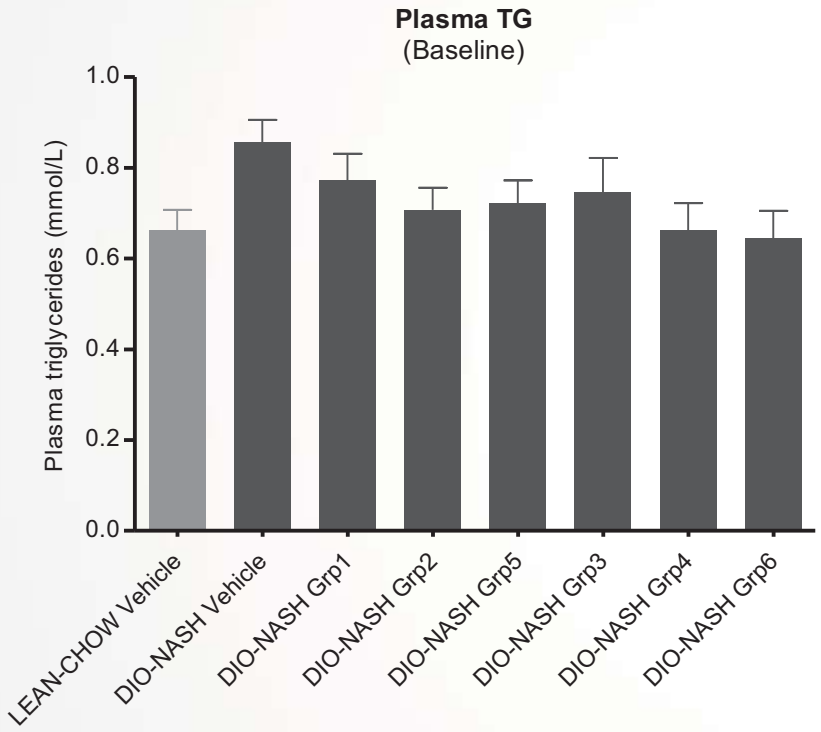
Baseline – Plasma liver enzymes

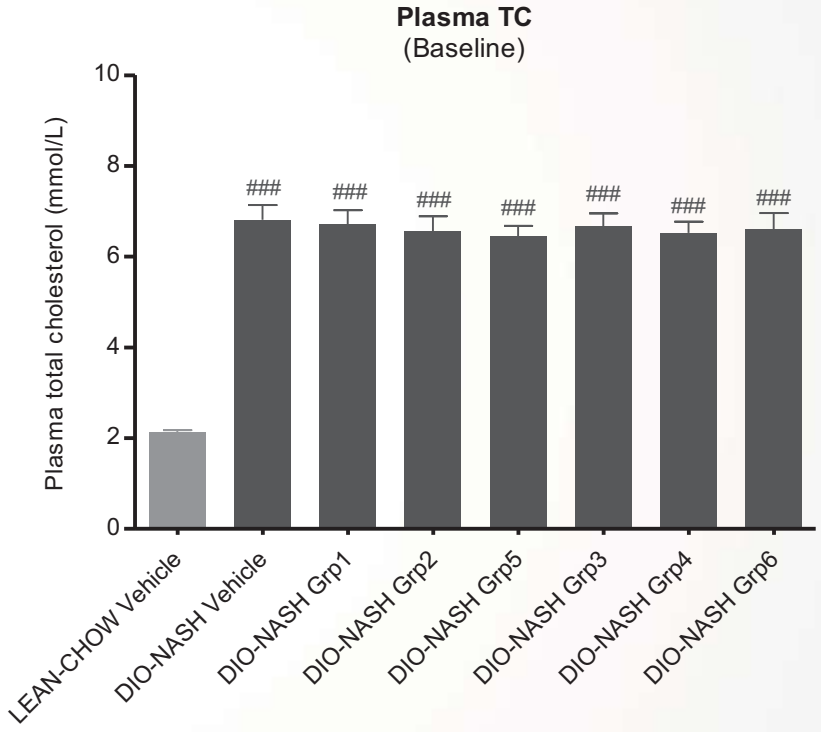




Elevated plasma liver enzymes

Baseline – Plasma lipids

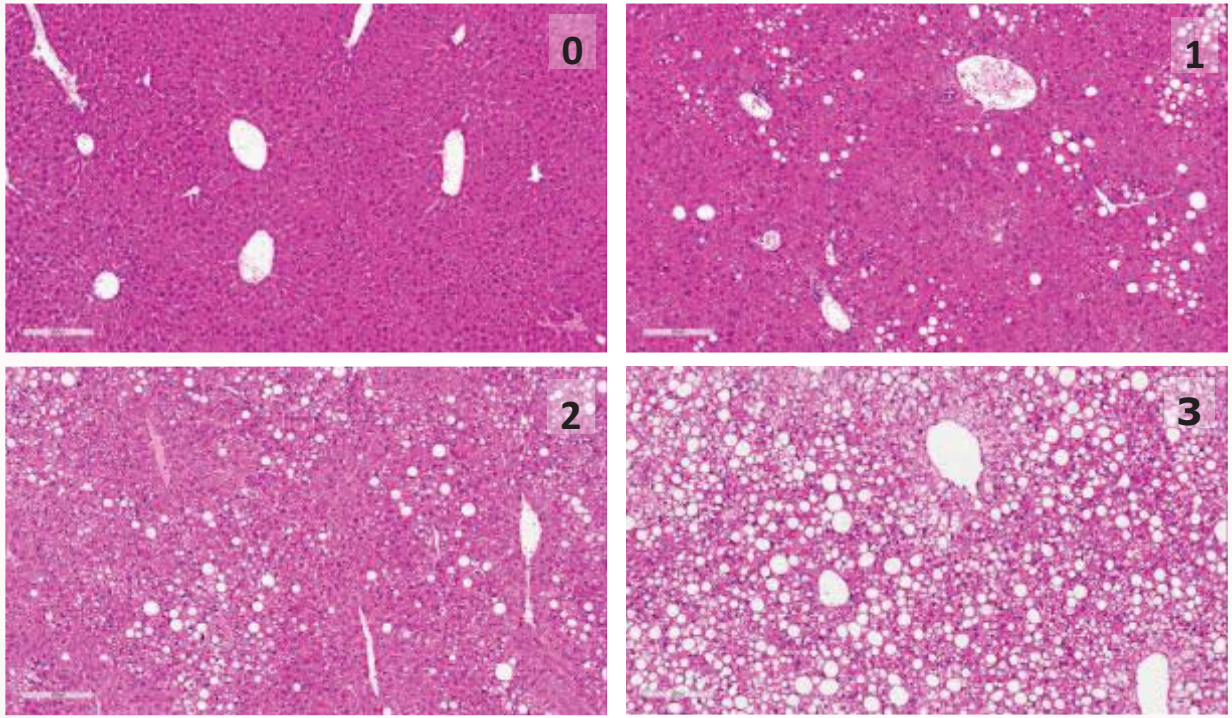




No hypertriglyceridemia, but hypercholesterolemia

NAFLD Activity Score - Steatosis

Steatosis stages represented in present study

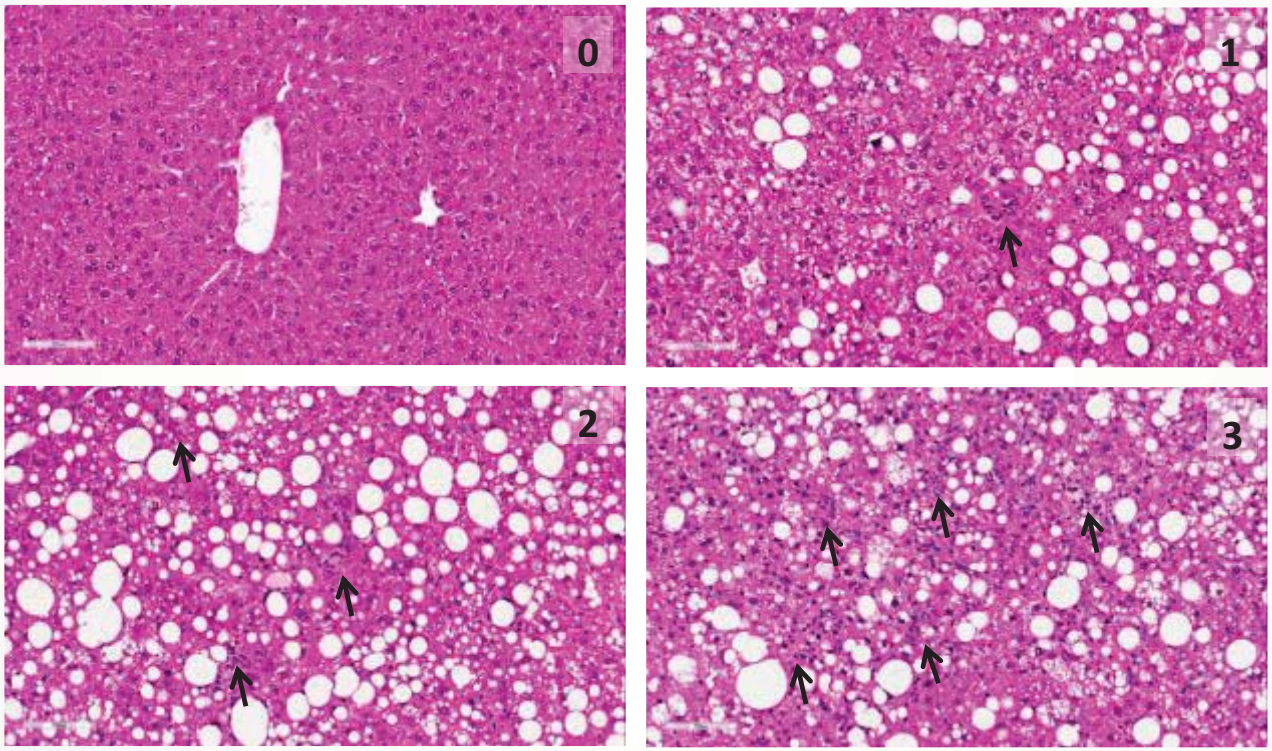


Steatosis score:

0: 0-5% steatosis; 1: >5-33% steatosis; 2: 34-66% steatosis; 3: >66% steatosis

NAFLD Activity Score - Inflammation

Inflammation stages represented in present study

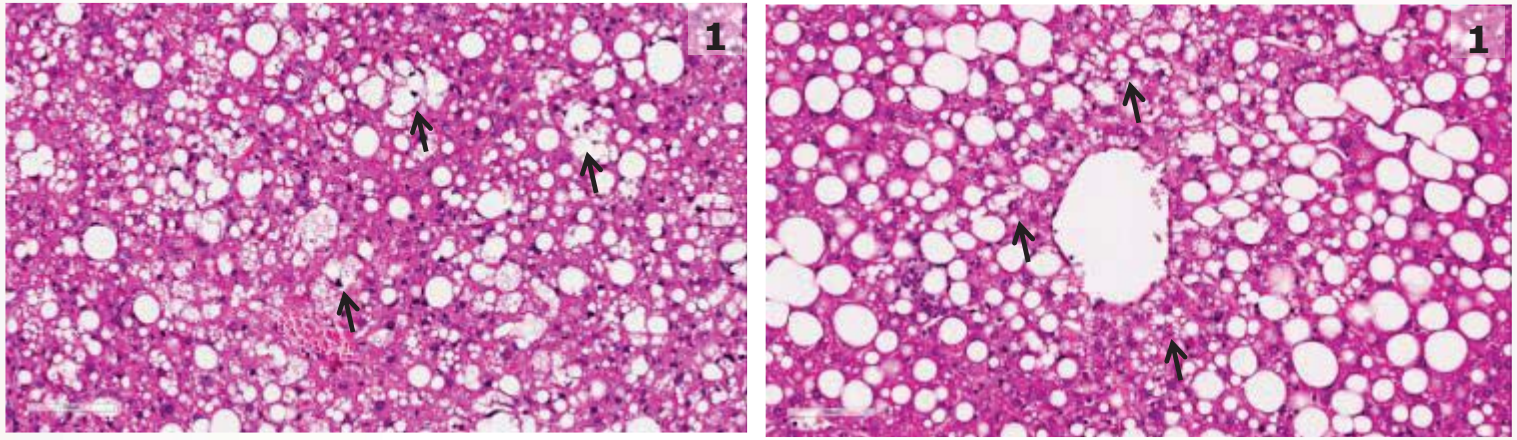


Lobular Inflammation:

0 = none; 1 = <2 foci per x 200 field; 2 = 2-4 foci per x 200 field; 3 = >4 foci per x 200 field

NAFLD Activity Score – Ballooning degeneration

Ballooning stages represented in present study

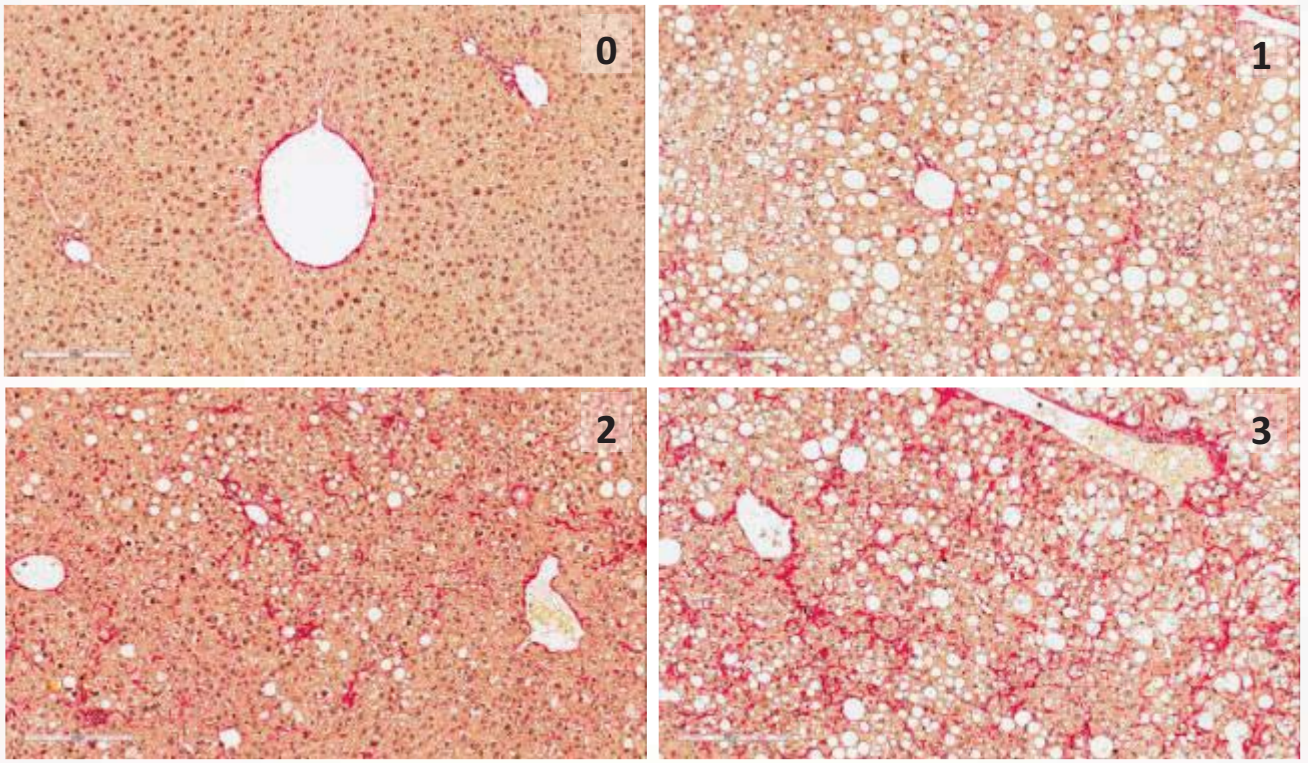


Hepatocyte ballooning:

0 = none; 1 = few ballooned cells

Fibrosis stage

Fibrosis stages represented in the present study

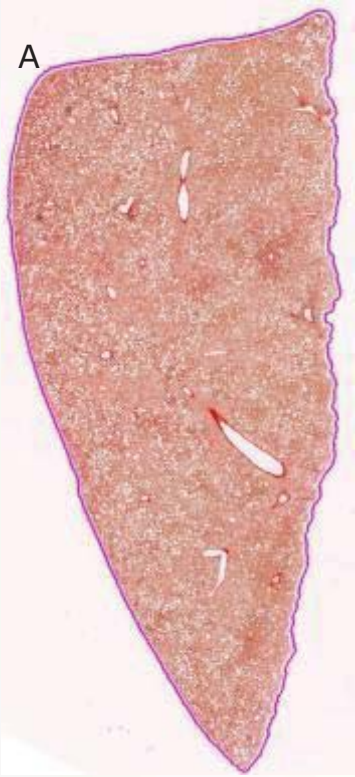


Fibrosis stage:

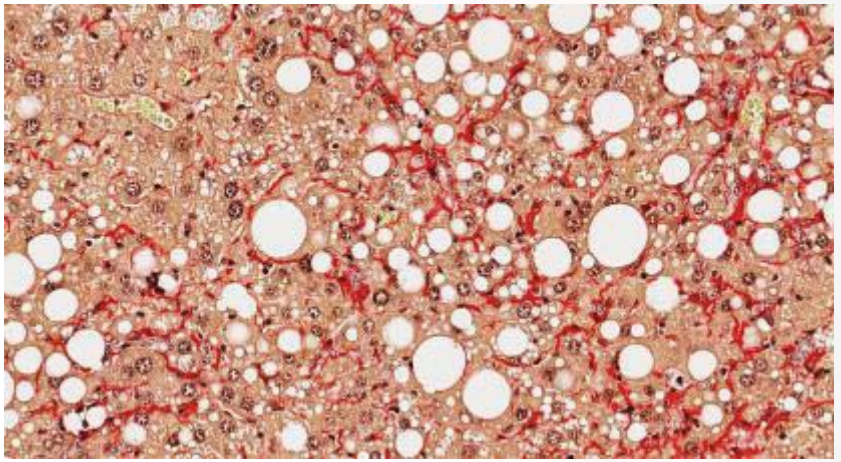
0: none; 1: perisinusoidal or periportal; 2: perisinusoidal and portal/periportal fibrosis; 3: bridging fibrosis

Whole slide image analysis - fibrosis

A



B



C

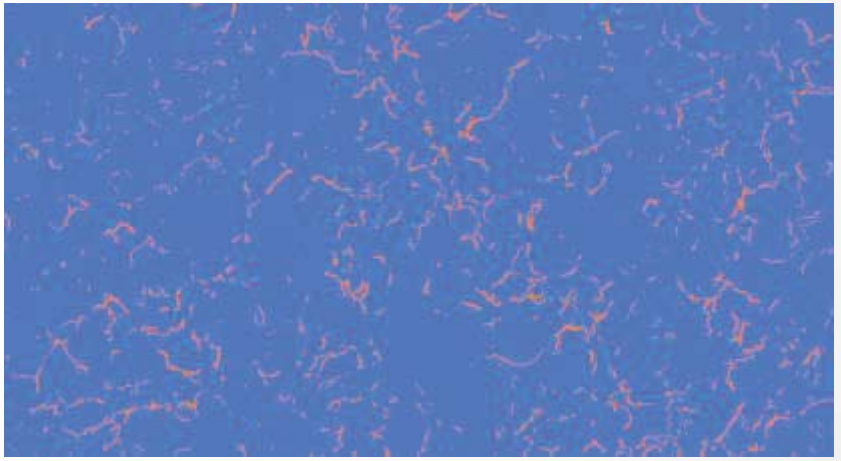


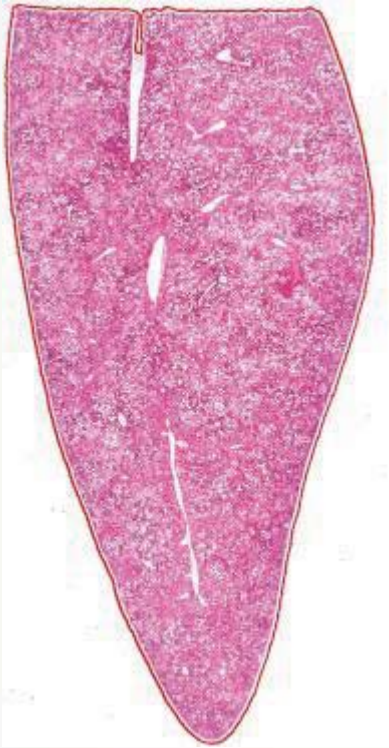
Image analysis

Quantification of fibrosis was done by image analysis from Sirius red staining. Scanned slides were analyzed in two steps:

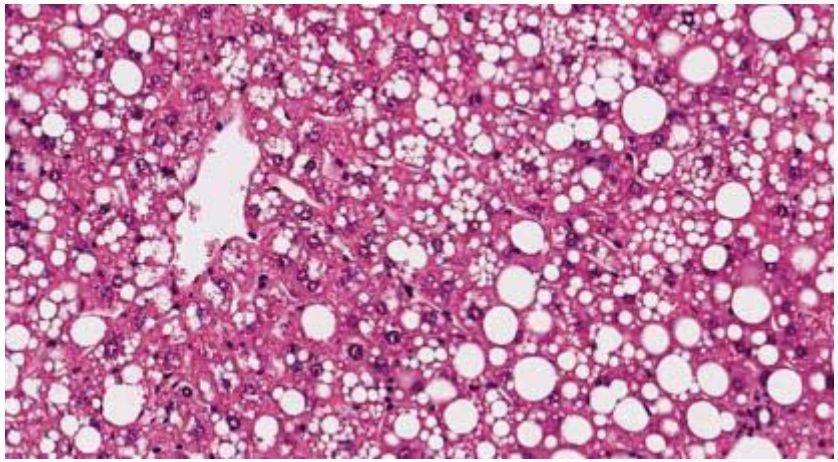
(1) Crude detection of tissue at low magnification (A). (2) Detection of collagen (red) and tissue (blue) at high magnification (B).

Whole slide image analysis - steatosis

A



B



C

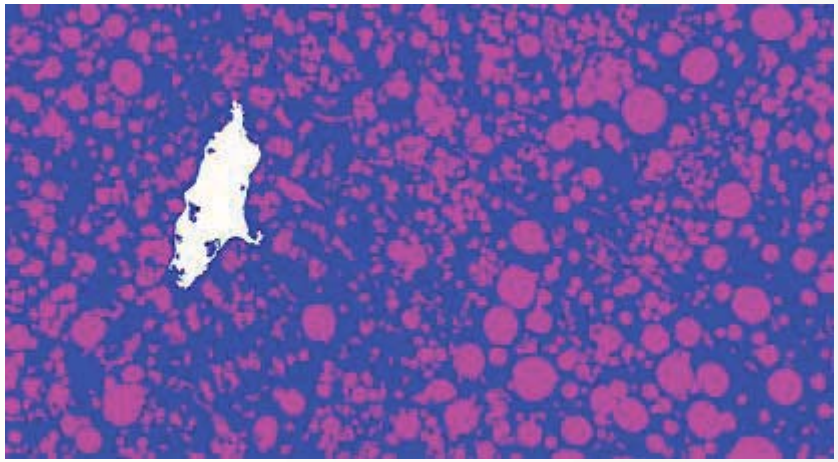


Image analysis

Quantification of steatosis by image analysis from H&E staining. Scanned slides were analyzed in two steps:

(1) Crude detection of tissue at low magnification (A).
(2) Detection of steatosis (pink) and tissue (blue) at high magnification (C).