UCLouvain, Belgium, Institut De Recherche Expérimentale Et Clinique, Laboratory of Hepato-Gastroenterology, [2] KU Leuven, Belgium, Department of Imaging and Pathology, [3] Antwerp University Hospital, Belgium, Department of Gastroenterology and Hepatology, [4] UCLouvain, Belgium, Institute of Neuroscience, Laboratory of Cell Physiology, [5] UCLouvain, Belgium, Institut De Recherche Expérimentale et Clinique, Endocrinology, Diabetology, and Nutrition Department, [6] UCLouvain, Belgium, IREC Imaging Platform, [7] Antwerp University Hospital, Belgium, Department of Radiology, [8] Cliniques universitaires Saint-Luc, Brussels, Belgium, Service d'hépato-Gastro-Entérologie, [9] Antwerp University, Belgium, Laboratory of Experimental Medicine and Pediatrics - Division of Endocrinology.

Introduction : A substantial body of literature supports that a low muscle mass, low strength or a higher muscle fatty infiltration are associated with NAFLD presence and severity. However, whether these muscle alterations are mere consequences of NASH, whether changes in the muscle compartment might be a signature of hepatocellular damages and inflammation, and whether these changes might play a pathophysiological role in NAFL to NASH transition remain hypothetical.

Aim : To investigate muscle changes in correlation with liver disease progression in NAFLD rodent models and in a human cohort.

Methods : For over 34 weeks, we followed WT mice fed a standard chow as controls (Ctl), WT mice fed a high fat (HF) diet (60% fat) as a model of simple steatosis (WT HF) and foz/foz mice fed a HF diet as a model of progressive NASH (FOZ HF). We developed and validated a novel preclinical micro-Computed Tomography (micro-CT) based methodology to prospectively study skeletal muscle mass and fatty infiltration in muscle and liver in a high-throughput and non-invasive manner. We used grip strength test to evaluate muscle functionality and analyzed liver histology at monthly intervals. We used CT to measure skeletal muscle mass and fatty infiltration retrospectively in a large cohort of 197 morbidly obese patients with biopsy proven NASH (n=117, 62.4%), NAFL (n=35, 18.9%) or normal liver histology (n=33, 17.8%). All data are mean±SEM.

Results : WT ND mice had normal liver histology at all times; WT HF mice developed modest steatosis at late time points; all FOZ HF had NAS >5 as from W12, with minimal fibrosis at W20 and patent pericellular fibrosis at W34. In FOZ HF with NASH, muscle mass dissociated from body weight gain. The relative decrease in muscle mass was associated with severe loss of muscle strength from W12 on (Ctl : 244±4g; WT HF : 251.9±6g vs FOZ HF : 228.6±4g) which further worsened with time (165.2±5.2g at 34W in FOZ HF). This was not seen in the other groups. Myosteatosis was the earliest muscular change as reflected by a significantly lower muscle density in FOZ HF as early as 4 week (0.79±0.02) when compared to Ctl (0.91±0.02) and reached a minimum at 12W (0.37±0.05 in FOZ HF vs 0.85±0.02 and 0.75±0.02 in Ctl and WT HF) then plateaued. Myosteatosis severity in FOZ HF, unexplained by body weight gain, was strongly correlated with NAS score ($r=-0.87$, $n=67$, $p<0.001$), irrespectively of the time point studied. Importantly, myosteatosis powerfully discriminated NASH from isolated steatosis or normal liver (AUROC = 0.96, $p<0.001$) in this model. In a large population of 185 morbidly obese patients, the CT-based psoas density index (reflecting myosteatosis) was significantly lower ($p<0.01$) in patients with NASH F-0,1 (1.44±0.03) and NASH F2+ (1.41±0.08) than in those with isolated steatosis (1.69±0.05) or normal liver histology (1.74±0.04). PDI identified patients with biopsy proven NASH amongst those with uncomplicated steatosis and normal liver histology with a good diagnostic performance (AUROC = 0.74, $p<0.001$), outperforming classical biomarkers such as FIB4, NFS and CK18 (AUROC = 0.57, 0.52 and 0.55 respectively). Furthermore, PDI and ALT levels were the only independent factors predicting NASH in a multivariate statistical model with associated AUROC of 0.81 ($p<0.001$).

Conclusions : Our data support that in NAFLD, hepatocellular damage and inflammation that characterize progression to NASH associate with myosteatosis. This observation paves the way for the exploitation of myosteatosis as a non-invasive marker of NASH and suggesting a muscle-liver reciprocal crosstalk during liver disease progression.

- A12 -

HEPATITIS E VIRUS GENOTYPE 3 SUBTYPE DEPENDENT CLINICAL OUTCOMES IN BELGIUM 2010-2018.

T. De Somer (1), M. Peeters (2), S. Klamer (3), F. Nevens (4), J. Delwaide (5), P. Stärkel (6), P. Willems (7), S. De Maeght (8), C. Moreno (9), M. Van Hoof (10), I. Colle (11), F. Sermon (12), C. Van Steenkiste (13), F. Janssens (14), J. Van Acker (15), A. Marot (16), E. Bottieau (17), M. Reynders (18), C. De Galocsy (19), L. Lasser (20), M. Steverlynck (21), J. Maus (22), W. Verlinden (23), A. Geerts (24), M. Gallant (25), S. Van Outryve (26), H. Reynaert (27), J. Mulkay (28), J. Decaestecker (29), V. Suin (2), S. Negrin-Dastis (30), S. Van Gucht (2), T. Vanwolleghem (1) / [1] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Gastroenterology & Hepatology, [2] Sciensano, Brussels, Belgium, National Reference Centre of Hepatitis Viruses, Viral Diseases, Infectious Diseases in Humans, [3] Sciensano, Brussels, Belgium, Epidemiology of Infectious Diseases, [4] UZ Leuven, Leuven, Belgium, Gastroenterology & Hepatology, [5] CHU of Liège, Belgium, Gastroenterology & Hepatology, [6] Cliniques universitaires Saint-Luc, Brussels, Belgium, Gastroenterology & Hepatology, [7] Sint Augustinus Ziekenhuis GZA, Antwerp, Belgium, Clinical Biology, [8] Centres Hospitaliers Jolimont, Belgium, Gastroenterology & Hepatology, [9] Hopital Erasme, ULB, Belgium, Gastroenterology & Hepatology, [10] Clinique Saint-Luc Bouge, Namur, Belgium, Gastroenterology & Hepatology, [11] ASZ, Aalst, Belgium, Gastroenterology & Hepatology, [12] OLV Aalst, Aalst, Belgium, Gastroenterology & Hepatology, [13] AZ Maria Middelares, Ghent, Belgium, Gastroenterology & Hepatology, [14] Jessa Ziekenhuis, Hasselt, Belgium, Gastroenterology

& Hepatology, [15] AZ Sint-Lucas, Ghent, Belgium, Clinical Microbiology, [16] CHU UCL Namur, Yvoir, Belgium, Gastroenterology & Hepatology, [17] Institute of Tropical Medicine Antwerp, Antwerp, Belgium, Internal Medicine Infectious Diseases, [18] AZ Sint-Jan Brugge-Oostende, Brugge, Belgium, Medical Microbiology, [19] Hôpitaux Iris Sud, Brussels, Belgium, Gastroenterology & Hepatology, [20] CHU Brugmann, Brussels, Belgium, Gastroenterology & Hepatology, [21] CENTRE HOSPITALIER MOUSCRON, Mouscron, Belgium, Gastroenterology & Hepatology, [22] ZNA Middelheim, Antwerpen, Belgium, Gastroenterology & Hepatology, [23] AZ Nikolaas, Sint-Niklaas, Belgium, Gastroenterology & Hepatology, [24] UZGent, Gent, Belgium, Gastroenterology & Hepatology, [25] Jan Yperman Hospital, Ieper, Belgium, Gastroenterology & Hepatology, [26] GZA Sint-Vincentius ziekenhuis, Antwerpen, Belgium, Gastroenterology & Hepatology, [27] UZBrussel, Brussel, Belgium, Gastroenterology & Hepatology, [28] CHU Saint-Pierre, Brussels, Belgium, Gastroenterology & Hepatology, [29] AZ Delta, Roeselare, Belgium, Gastroenterology & Hepatology, [30] Grand Hôpital de Charleroi, Charleroi, Belgium, Gastroenterology & Hepatology.

Introduction : Hepatis E Virus (HEV) infections are emerging in the Western civilization with a predominance of HEV genotype 3 (gt3). Except for immunosuppression, male gender, age older than 50 years and chronic liver disease, no correlators with clinical outcomes of a HEV gt3 infection have been identified. In Belgium, diagnosis of HEV is centralized at the National Reference Center (NRC) for Viral Hepatitis, Sciensano.
Aim : We analyzed virological factors and clinical outcomes in a nationwide cohort of HEV patients in Belgium with the aim of finding other correlators with clinical outcomes.
Methods : Demographic, clinical and biochemical parameters of HEV infections documented at the NRC Sciensano between 2010 and 2018 were collected. Serum HEV-IgM, -IgG and HEV RNA were determined by ELISA and RT qPCR. HEV was subtyped by Sanger sequencing of an ORF2 fragment. Odds ratios (OR), risk ratios (RR) and 95% confidence intervals (95% CI) were calculated using STATA.
Results : 402 cases were identified. Among 300 cases with clinical data, the median age was 57 years and 69% of patients were males. HEV viremia was detected in 211 patients with a genotype identified in 177 patients. HEV gt3 infections largely predominate (93% [165/177]) with subtypes 3c (38% [67/177]) and 3f (44% [78/177]) almost equally represented. The percentage of immunocompromised patients was higher for patients infected with a virus from the clade of gt3c (achi), compared to a virus from the clade of gt3f (efg) (30% vs 16%; OR3c=2.2 [1.0-4.7] p=0.045). A similar, however non-significant trend was observed for patients with pre-existing liver cirrhosis (9.9% vs 3.4%; OR3c=3.1 [0.8-12.5]). Biochemically, patients with a HEV gt3f infection had higher ALT peak values and higher peak bilirubin values compared to patients with a HEV gt3c infection (respectively mean of 2199 vs 1528 U/L; p=0.005 and mean of 8.6 vs 4.1 mg/dl; p=0.001). In addition, patients with a HEV gt3c infection were treated more frequently in ambulatory care settings compared to patients with a HEV gt3f infection. The percentage of patients admitted to the hospital was higher for patients with a HEV gt3f infection compared to patients with a HEV gt3c infection (61% vs 36%; RR3f=1.7 [1.2-2.4] p=0.003). There were no differences between the subtypes in intensive care unit admissions (5.7%), in hospitalization durations (median of 4.0 weeks), in chronicity (18% vs 14%, RR3f=0.8 [0.4-2.0]), nor in deaths (1.4% vs 4.8%; RR3f=3.4 [0.4-30]).
Conclusions : A similar number of HEV gt3c and gt3f infections have been diagnosed in Belgium. Despite more pre-existing comorbidity in patients infected with HEV gt3c, HEV gt3f infections are associated with a more severe disease course according to laboratory values and hospitalization rates. Our nationwide analysis is the first to identify a correlation between HEV gt3 subtype and clinical outcomes.

- A13 -

TRANSCRIPTOME PROFILING OF LIVER BIOPSIES BEFORE ANTIVIRAL TREATMENT START CAN PREDICT HCC DEVELOPMENT 8.3 YEARS BEFORE CLINICAL DIAGNOSIS IN CHRONIC HEPATITIS B AND C PATIENTS. S. Van Hees (1), B. Cuypers (2), S. Bourgeois (3), K. Kreefft (4), D. Sprengers (5), G. Robaeys (6), P. Meysman (2), L. Vonghia (1), P. Michielsen (1), S. Francque (1), R. De Man (4), A. Driessen (7), A. Boonstra (4), K. Laukens (2), T. Vanwolleghem (1) / [1] Antwerp University Hospital, Belgium, Department of Gastroenterology and Hepatology, [2] Antwerp University, Belgium, Department of Mathematics and Computer Science, [3] ZNA Stuivenberg, Borgerhout, Belgium, Department of Gastroenterology and Hepatology, [4] Erasmus Medical Center, Rotterdam, Netherlands (the), Department of Gastroenterology and Hepatology, [5] GZA Antwerp, Belgium, Department of Gastroenterology and Hepatology, [6] Hospital East-Limburg, Belgium, Department of Gastroenterology and Hepatology, [7] Antwerp University Hospital, Belgium, Department of Pathology.

Introduction : An accurate prediction of Hepatocellular Carcinoma (HCC) development in Chronic Hepatitis B (CHB) and C (CHC) patients is currently impossible.
Aim : In this study we explored pre-antiviral treatment liver transcriptome profiles of CHB and CHC patients with and without HCC development during long-term follow-up and investigated their potential to predict future HCC development.
Methods : HCC developing cases (n = 34) were identified through retrospective chart review of all CHB and CHC patients with an available pre-antiviral treatment liver biopsy from 5 large Hepatology clinics. Cases were split in 4