there is a paucity of data on the impact of progression to cirrhosis on patient reported outcomes (PRO) and health related quality of life (HRQOL). The aim of this study was to perform a prospective, cross-sectional analysis of MASLD-specific PRO in patients with MASLD in a real-world setting.

Method: A prospective analysis of the NASH-CHECK PRO in the real-world TARGET-NASH observational longitudinal ongoing cohort in patients enrolled in the United States at academic and community sites was performed from 2021 to 2023. PRO and HRQOL were evaluated in a subset of participants using the NASH-CHECK instrument (version 1.0) that was developed and validated per regulatory guidance. MASLD was defined per the TARGET-NASH definitions using available biopsy, imaging, and clinical criteria as described previously. Three categories of patients were compared using previously published and validated case-definitions: (1) MASL, (2) MASH, (3) MASH cirrhosis. NASH-CHECK has 6 symptom scale scores and three additional HRQOL scores; each has a score of 0–10 with higher scores indicating greater impairment. Scores across classes were compared using ANOVA. A p value < 0.05 was considered significant.

Results: Data from 801 participants with a completed NASH-CHECK PRO and MASLD were obtained (n = 249, 296, 256 for MASL, MASH, and MASH cirrhosis respectively). Median age was 62, 61% female, 81% Non-Hispanic White, 7% Non-Hispanic Black, 7% Hispanic/Latino, 65% obese (BMI ≥ 30), 22% cardiovascular disease, 80% hypertension, 61% type 2 diabetes, 72% dyslipidemia, median follow-up 68 months. Significant differences were noted between MASL, MASH, and MASH cirrhosis: $p < 0.001$ for itchy skin, activity limitation, emotional impact, social impact; $p = 0.011$ for fatigue; $p = 0.018$ for cognitive impact. Scores for those with MASH cirrhosis were significantly higher than MASL and MASH for all domains except abdominal pain, abdominal bloating, and sleep.

Conclusion: In a real-world clinical setting, the recently validated MASLD-specific PRO measure instrument, NASH-CHECK, demonstrated significantly worse scores in patients with MASH cirrhosis vs those with MASL or MASH in 6 out of 9 domains.

FRI-223

Cost-effectiveness of one-time screening for advanced hepatic fibrosis using FIB-4 based two-step algorithm in the general population

Eileen Yoon[1], Jihyun An[2], Ha Il Kim[3], Joo Hyun Sohn[3], Bo-Kyeong Kang[4], Eun Chul Jang[5], Huiyul Park[6], Hye-Lin Kim[7], Sang Bong Ahn[8], Joo Hyun Oh[9], Dae Won Jun[10]. *[1]Department of Internal Medicine, Hanyang University, Seoul, Korea, Rep. of South; [2]Department of Internal Medicine, Hanyang University, Guri, Korea, Rep. of South; [3]Department of Internal Medicine, Hanyang University College of Medicine, Guri, Korea, Rep. of South; [4]Department of Radiology, Hanyang University College of Medicine, Seoul, Korea, Rep. of South; [5]Department of Occupational and Environmental Medicine, Soonchunhyang University College of Medicine, Chun An, Korea, Rep. of South; [6]Department of Family Medicine, Myoungji Hospital, Hanyang University College of Medicine, Goyangsi, Korea, Rep. of South; [7]College of Pharmacy, Sahmyook University, Seoul, Korea, Rep. of South; [8]Department of Internal Medicine, Nowon Eulji Medical Center, Eulji University, College of Medicine, Seoul, Korea, Rep. of South; [9]Department of Internal Medicine, Nowon Eulji Medical Center, Eulji University, College of Medicine, Seoul, Korea, Rep. of South; [10]Department of Internal Medicine, Hanyang University College of Medicine, Seoul, Korea, Rep. of South*
Email: noshin@hanyang.ac.kr

Background and aims: There is currently inadequate evidence supporting one-time screening and intensive lifestyle modification for advanced fibrosis in the general population. Therefore, this study is designed to assess the cost-effectiveness of a screening strategy utilizing the FIB-4 test followed by vibration-controlled transient elastography (VCTE) for identifying advanced hepatic fibrosis within the general United States population.

Method: We constructed a combined model of the decision tree model and Markov model to compare expected costs and quality-adjusted life-years (QALYs) between 'screening' and 'no screening' groups from healthcare system perspectives. Cardiovascular disease (CVD) conditions, which have the potential combined with advanced hepatic fibrosis, were also incorporated into the model. Patients diagnosed with advanced fibrosis in the screening group were given intensive lifestyle intervention (ILI). The incremental cost-effectiveness ratio (ICER) was calculated for a 30-year horizon.

Results: ICERs of one-time screening for advanced hepatic fibrosis using FIB-4 based two-step algorithm in the general population in their 40 s was $69, 242 per QALY, respectively, which was under the $100, 000, regarded as an ICER threshold in the US, indicating that screening is cost-effective. However, those before their 30 s and after 60 s exceeded the threshold. The most influential parameters on cost-effectiveness were the ILI success rate and duration of ILI. If the success rate of ILI drops to less than 28% (as fibrosis regression rate, 14.1%), cost-effectiveness was disappeared.

Conclusion: Screening for detecting advanced hepatic fibrosis using FIB-4 based two-step algorithm followed by ILI was cost-effective in the general population with 40 s.

FRI-224

Intramyocellular lipids are associated with insulin resistance in metabolic dysfunction-associated steatotic liver disease

Guillaume Henin[1,2], Maxime Nachit[2], Harmen Reyngoudt[3], Etienne Danse[4], Pierre Trefois[4], Frank Peeters[4], Salomé Declerck[2], Stéphanie André-Dumont[1], Alexis Goffaux[2], Benjamin Marty[3], Isabelle Leclercq[2], Audrey Loumaye[5], Nicolas Lanthier[1,2]. *[1]Service d'Hépato-gastroentérologie, Cliniques universitaires Saint-Luc, UCLouvain, Brussels, Belgium; [2]Laboratory of Hepatogastroenterology, Institut de Recherche Expérimentale et Clinique, UCLouvain, Brussels, Belgium; [3]Institute of Myology, Neuromuscular Investigation Center, NMR laboratory, Paris, France; [4]Service de Radiologie, Cliniques universitaires Saint-Luc, UCLouvain, Brussels, Belgium; [5]Service d'Endocrinologie, diabétologie et nutrition, Cliniques universitaires Saint-Luc, UCLouvain, Brussels, Belgium*
Email: nicolas.lanthier@saintluc.uclouvain.be

Background and aims: Insulin resistance is considered an indicator of the severity of MASLD. In this context, the role of skeletal muscle fat and its intra- or extra-myocellular localisation on insulin sensitivity remains debated. The aim of this study is to assess muscle lipid content and cellular localisation using proton-magnetic resonance spectroscopy (^{1}H-MRS) and its relationship with insulin resistance in a cohort of MASLD subjects.

Method: MASLD patients were prospectively recruited based on the co-existence of liver steatosis measured by a controlled attenuation-parameter (CAP) above 251 dB/m and at least one cardiometabolic risk factor. Type 2 diabetes was defined by the intake of hypoglycemic drugs. Insulin resistance was estimated in non-diabetic patients using the homeostatic model assessment of insulin resistance (HOMA-IR). Intra (IMCL) and extramyocellular lipids (EMCL) were measured in vivo using ^{1}H-MRS. Single voxel ^{1}H-MRS was performed on a 3-Tesla Signa Premier scanner (GE healthcare) on tibialis anterior (TA) and soleus using a PRESS-sequence (voxel size $10 \times 10 \times 15$ mm^3, TE = 27 ms, TR = 1500 ms, 8 averages). JMRUI software, including the AMARES algorithm was used to quantify IMCL and EMCL on non-water suppressed spectra.

Results: 54 MASLD patients were included. 32 patients were male (59%), with a mean age of 54 years (range: 19–75). 27 patients were diabetic (50%). Mean BMI was 35 (range: 24–60). Mean waist circumference was 118 cm (range: 89–160). Mean CAP and liver elasticity were 342 dB/m (range: 242–400) and 14.8 kPa (range: 3.6–35). In the entire cohort, mean TA lipid content was 0.6% for IMCL (range: 0.1–1.5) and 1.8% (0.3–6.8) for EMCL ($p < 0.05$). Mean soleus

lipid content was 0.8% for IMCL (range: 0.2–2.1) and 4.4% for EMCL (range: 0.3–10.9) ($p < 0.05$). In non-diabetic patients, mean fasting glycaemia was 103 mg/dl (range: 76–126) and mean HOMA-IR was 8 (range: 1.7–26). The HOMA-IR index was positively correlated to IMCL content in the TA ($r = 0.63$, $p = 0.017$) but no correlation was found with EMCL content or with soleus fat content (IMCL and EMCL). Diabetic patients had a higher IMCL content in the soleus compared to non-diabetic patients (0.9% versus 0.6%; $p = 0.02$). No difference was highlighted for the EMCL content of soleus (4.1% versus 4.7%; $p > 0.05$) or for IMCL for TA (0.55% versus 0.7%; $p > 0.05$) between diabetic and non-diabetic patients.

Conclusion: The majority of skeletal muscle lipids are extramyocellular. However, IMCL but not EMCL content assessed by ^{1}H-MRS positively correlates with insulin resistance assessed by the HOMA-IR index in non-diabetic MASLD patients. This observation is reinforced by the IMCL content in diabetic patients being significantly higher compared to non-diabetic patients. This observation highlights a link between IMCL, systemic insulin resistance and type 2 diabetes in MASLD.

FRI-225

Novel digital pathology adequacy score benchmarks the performance of pre-analytical method for digital pathology and AI end-to-end tissue assays

Louis Petitjean[1], Li Chen[2], Adi Lightstone[2], Nathan Aist[2]. *[1]PharmaNest, Inc, Princeton, United States; [2]PharmaNest Inc, Princeton, United States*
Email: louis.petitjean@pharmanest.com

Background and aims: The control and monitoring of pre-analytical conditions is key to minimize the noise and variability of Digital Pathology read-outs in the context of Artificial-enabled Digital Pathology tissue assay used for the assessment of liver biopsies. While modern AI algorithms can compensate for most sources of noise (FibroNest, doi: 10.1111/liv.15768), additional opportunities can be addressed for large studies. Inspired by the definition of Adequacy for tissue biopsies, we report the development, validation, and results of a Digital Biopsy Adequacy (DBA) score as a Key Performance Indicator (KPI) to measure liver biopsy pre-analytical quality.

Method: The BDA score is a normalized composite score (1 to 10) to evaluate a digital pathology image along three dimensions and 24 features including (i) Biopsy tissue and glass slide processing (11 features such as area of the biopsy, tissue rupture, folding artifacts) (ii) staining quality (7 features including over or under staining, rinsing artefacts) and (iii) digital scanning (6 features including out-of-focus areas, scanning stripes). The score is based on a point-based method where defects have different penalty weights, such as one single defect can significantly affect the overall score. The method is consistent with the August 2021 FDA Guidance to Industry and Technical Specifications for Submission of Clinical Trials Data Sets for Treatment of NASH, Bio specimen Findings (BS) domain. Digital Pathology images are classified as Non-Adequate ($DBA < 5$), Minimally Acceptable ($5 < DBA < 8$) and Acceptable ($BDA > 8$). We report aggregated DBA results for N = 5227 Digital images processed since 2020 from 13 Phase 2 and 3 MASH studies.

Results: From one operator scoring 385 images and a second independent operator scoring a random subset of 99 images, the Intra-Class Correlation (ICC) is 0.876 ("excellent," Cichetti, 1994) and the Linear Correlation is 0.889 ("good," Koo and Li, 2016). We observe significantly different Not Acceptable ratios (Min 0%, Mean 8%, Median 6% Std 10% Max 41%) and Acceptable Ratios (35%, 71%, 79%, 19%, 97%) across studies. The main toot causes for non and minimal adequacy are overstaining, sectioning and folding artefacts, which can be resolved by basic quality control procedures and rework. Best in class performers demonstrate non-acceptable images can be fully avoided.

Conclusion: The use of a KPI for pre-analytical quality in a Digital Pathology end-to-end tissue assay has the potential to significantly improve the Digital Pathology Images used in MASH studies. The industry benchmark (13 studies, 5227 images) demonstrates that defect rates (not-acceptable biopsies) can be realistically expected to be below 3% and that the rate of fully adequate digital images be above 80%. This KPI should be used to incentivize some pre-analytical laboratories to implement basic Quality Assurance and rework processes.

FRI-226

The impact of light to moderate alcohol consumption on liver and cardiovascular damage in metabolic-dysfunction associated steatotic liver disease

Rosa Lombardi[1], Felice Cinque[1], Andrea Dalbeni[2], Annalisa Cespiati[1], Floriana Santomenna[1], Jaqueline Currà[1], Daniel Smith[1], Erika Fatta[1], Cristina Bertelli[1], Giuseppina Pisano[1], Edoardo Pulixi[1], Anna Mantovani[2], Mirko Zoncapè[2], David Sacerdoti[2], Anna Ludovica Fracanzani[1]. *[1]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico of Milan, University of the Study of Milan, Milan, Italy; [2]University of Verona and University and Hospital Trust (AOUI) of Verona, Verona, Italy*
Email: rosalombardi@hotmail.it

Background and aims: Metabolic-dysfunction associated steatotic liver disease (MASLD) and met-ALD are both characterized by hepatic fat and metabolic alterations without other causes of liver disease but the amount of daily alcohol consumption in their definition differs (0–30/0–20 die vs 30–60/20–50 g/die male/female). MASLD and met-ALD expose patients to progressive liver disease and increased cardiovascular (CV) risk, however the impact of the amount of alcohol in this setting needs to be elucidated. Aim: to evaluate the impact of light alcohol consumption in MASLD on the hepatic and CV damage in a multicentric cohort of steatotic patients with metabolic alterations as compared to total abstinence and met-ALD

Method: 729 patients with ultrasound (US) proven steatosis (mean age 52 ± 12 years, 77% male) without other causes of liver disease were enrolled and classified according to their drinking habits as abstainers (0 g/die) and light consumers in MASLD (<30/20 g/die male/female) or met-ALD (30–60/20–50 g/day male/female). Steatosis was graded by US, hepatic fibrosis diagnosed by LSM > 8.0 kPa at Fibroscan, CVD by carotid US (cIMT > 0.9 mm, plaques) and echocardiography (systolic and diastolic function, epicardial adipose tissue EAT > 7.5/9.5 mm M/F).

Results: 397 (54%) were no alcohol consumers (NAC-MASLD), 290 (40%) light alcohol consumers (LAC-MASLD) and 42 (6%) met-ALD. Considering LAC-MASLD vs NAC-MASLD, there was no difference in the severity of liver disease (severe US steatosis 22% vs 16% $p = 0.06$, LSM > 8 kpa 9% vs 9%, $p = 0.89$). Conversely, LAC had a significantly lower prevalence of cIMT > 0.9 mm compared to NAC (18% vs 28%, $p = 0.005$) and resulted an independent protective factor for increased cIMT (adjusted for age, sex, active smoking, T2DM, hypertension, dyslipidemia, overweight; OR 0.58, CI 95% 0.36–0.93). No difference in other CV parameters was observed. Considering LAC-MASLD vs met-ALD, the latter had significantly higher LSM values (6.4 ± 3.2 vs 5.4 ± 2.2, $p = 0.02$) despite a not significantly different prevalence of LSM > 8 kPa (19% vs 9%, $p = 0.10$). Met-ALD vs LAC-MASLD had a significantly higher prevalence of carotid plaques (55% vs 30%, $p = 0.003$) and resulted an independent risk factor for carotid plaques (adjusted for sex, active smoking, T2DM, hypertension, dyslipidemia, overweight, statins use; OR 2.01, CI 95% 1.00–4.12). Conversely, there was no difference in the prevalence of severe US steatosis or other CV parameters.

Conclusion: Light alcohol consumption in middle-aged MASLD patients appears to protect against early atherosclerosis without exhibiting more severe liver disease compared to abteiners. However, when alcohol consumption increases up to the level of met-ALD, the cardiovascular protection is hampered and alcohol becomes harmful also for the liver.