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COMORBIDITIES IN NAFLD – METABOLIC SYNDROME AND BEYOND, REPAIR STUDY INSIGHTS

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NAFLD and MetS

The relationship between NAFLD and MetS is well established; one meta-analysis of 20 trials (117,020 patients) demonstrated that the presence of NAFLD increased the risk of MetS, with an OR of 1.80 (95% CI 1.72; 1.89) compared with individuals without NAFLD.[1] There are various diagnostic criteria for MetS; the 2009 IDF-NHLBI-AHA-WHF-IAS-IASO Harmonized criteria define MetS as the presence of ≥3 factors out of elevated waist circumference, raised triglycerides, reduced HDL, high blood pressure, and elevated fasting plasma glucose.[2]

Whilst increased BMI and waist circumference are associated with insulin resistance and NAFLD (and are predictors of advanced disease), patients with NAFLD who are lean also display insulin resistance and altered body fat distribution.[3] Insulin resistance and T2DM correlate with fatty infiltration in the liver, and are strongly associated with increased NAFLD severity and progression to NASH.[4,5]

NAFLD and other comorbidities

In addition to metabolic-associated comorbidities, NAFLD is associated with an increased risk of cardiac comorbidities, including coronary artery disease, heart failure, coronary artery calcification, atrial fibrillation, and cardiovascular mortality.[6–12] NAFLD may also accelerate the development and progression of chronic kidney disease,[13] and increase the risk of neoplasia (including HCC).[14]

REPAIR study: study design and baseline characteristics[15]

The REPAIR study was a descriptive, cross-sectional, non-interventional, multicenter study conducted in 64 sites across five cities in the Republic of Kazakhstan. Outpatients aged 15–65 years with chronic viral hepatitis, hepatic steatosis, and diabetes- or obesity-related liver disease treated with EPL (based on physician decision) as an add-on to standard of care were recruited. Stage 1 of the study assessed the profile of patients receiving EPL treatment and physician prescribing practice (during Visit 1, patients provided informed consent for study participation, but no procedures beyond routine clinical practice were performed). During Stage 2, patients attended a second visit at Week 12, during which EPL adherence, tolerance, and treatment satisfaction were assessed.

A total of 1,505 patients met the inclusion criteria and were included in the analysis, of which 96.1% of patients completed the study per protocol. Median age was 49.9 years, and just over half (56.5%) of patients were female; median BMI was 30.6 kg/m^2 for women and 29.9 kg/m^2 for men.

REPAIR study: prevalence of chronic liver diseases and comorbidities[15]

Pathological signs of NAFLD were detected in 87.8% of patients who received liver biopsy. Of those patients, the proportion of chronic liver diseases were as follows: primary hepatic steatosis, 32.2%; obesity-induced liver disease, 25.8%; chronic viral hepatitis, 16.0%; T2DM-induced liver injury, 14.6%; and 'other', 11.4%. Metabolic comorbidities were common: 59.7% of patients had obesity, 58.8% had hypertension, 48.6% had dyslipidemia, and 24.0% had T2DM. Of the non-metabolic comorbidities, digestive disorders were most common (57%), followed by circulatory system disease (18.4%), and endocrine disease (5.7%).

REPAIR study: EPL treatment adherence and tolerance[15]

A total of 300 patients were invited to Stage 2 of the study, 80.3% of whom completed EPL treatment (median dose, 1,800 mg/day; median treatment duration, 12 weeks). Of the 19.7% of patients who did not finish treatment, most discontinuations were due to financial difficulties (36.8%) and improvement in their condition (31.6%). Only three, mild AEs were observed during the follow-up period; one patient experienced cholestasis and pruritis (which resolved completely), and one patient reported abdominal pain.

REPAIR study: patient and physician satisfaction with EPL treatment[15]

Most physicians and patients were satisfied with EPL treatment (mean [SD] satisfaction: 8.7 [1.7] and 9.0 [1.5], respectively). Of the 274 patients with known treatment outcomes, 31.4% of patients recovered completely from their liver condition, and 59.9% experienced significant improvement.

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AHA, American Heart Association; BMI, body mass index; CI, confidence interval; EPL, essential phospholipids; HCC, hepatocellular carcinoma; HDL, high-density lipoprotein; IAS, International Atherosclerosis Society; IASO, International Association for the Study of Obesity; IDF, International Diabetes Federation; MetS, metabolic syndrome; NAFLD, non-alcoholic fatty liver disease; NASH, non-alcoholic steatohepatitis; NHLBI, National Heart, Lung and Blood Institute; OR, odds ratio; SD, standard deviation; T2DM, type 2 diabetes mellitus; WHF, World Heart Federation.

Learning objectives:

- Understand the link between NAFLD and MetS
- Recognize the non-metabolic comorbidities with well-established or emerging links to NAFLD
- Identify the liver diseases and comorbidities of patients enrolled in the REPAIR study
- Gain an insight into EPL treatment adherence, tolerance, and patient and physician satisfaction in the REPAIR study

Main takeaways:

- There is a well-established relationship between NAFLD and MetS
- Patients with NAFLD are also at an increased risk of several non-metabolic comorbidities, including (but not limited to) cardiovascular disease, chronic kidney disease, and tumors (including HCC)
- The REPAIR study was a descriptive, cross-sectional, non-interventional, multicenter study conducted at 64 sites across five cities in the Republic of Kazakhstan (N=1,505)
    - A total of 87% of patients who received liver biopsy had had signs of liver disease (namely: primary hepatic steatosis, 32.2%; obesity-induced liver diseases, 25.8%; chronic viral hepatitis, 16.0%; T2DM-induced liver injury, 14.6%; and 'other', 11.4%)
    - Metabolic comorbidities were common (obesity, 59.8%; hypertension, 58.8%; dyslipidemia, 48.6%; T2DM, 24.0%). Of the non-metabolic comorbidities, digestive disorders were most frequently observed (57%)
    - Patients reported good tolerance, satisfaction with, and adherence to, EPL treatment; of the 274 patients with known treatment outcomes, 31.4% recovered from their condition and 59.9% noted substantial improvement

BMI, body mass index; EPL, essential phospholipids; HCC, hepatocellular carcinoma; HDL, high-density lipoprotein; MetS, metabolic syndrome; NAFLD, non-alcoholic fatty liver disease; T2DM, type 2 diabetes mellitus.

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