rates. This study aimed to elucidate the clinical course and practices of CCA in Latin America.

Patients / Materials and Methods: This observational cohort study investigated individuals diagnosed with CCA between 2010-2023 in five referral centers across Latin America. Demographic, biochemical, and clinical data were analyzed.

Results and Discussion: A total of 309 patients were enrolled, demonstrating a balanced distribution of CCA subtypes (intrahepatic, perihilar, and distal), with Hispanics and Caucasians as the predominant ethnic groups, followed by Africans. Major risk factors identified included age, diabetes, obesity, MASLD, bile duct stones, and cholecystitis. Disparities in overweight/obesity prevalence were noted among CCA subtypes and ethnicities, with higher rates in extrahepatic CCAs and among Hispanics and Caucasians. At diagnosis, 72% of patients had ECOG-PS scores of 0-1, with disease presentations ranging from localized (47%) to locally advanced (19%) and metastatic (34%). Patients who did not receive any anti-cancer therapy exhibited a median survival of 2.3 months. Survival rates significantly improved across treatment modalities, with surgery yielding the longest (34 months), followed by chemotherapy (8 months). Notably, Africans presented with worse ECOG-PS scores and more advanced disease, while Hispanics were less frequently treated with chemotherapy, contributing to lower survival rates.

Conclusions: The high prevalence of late-stage CCA diagnosis in Latin America, particularly among Africans, alongside a substantial proportion of Hispanic patients not receiving chemotherapy, underscores a dismal prognosis for patients. These findings highlight structural challenges in cancer screening and healthcare access among diverse ethnic backgrounds and lower socioeconomic statuses in the region. Urgent measures are warranted, including identifying preventable risk factors, increasing awareness among high-risk populations, and establishing equitable health coverage to address these disparities.

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OP- 14 ENHANCED MUSCLE MASS MITIGATES MASLD IN MYOSTATIN KNOCKOUT MICE WITHOUT IMPACTING EXERCISE PERFORMANCE

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Conflict of interest: No

Introduction and Objectives: Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) is linked to sarcopenia and exacerbated by obesity. Individuals with higher relative skeletal muscle mass are protected against MASLD or more likely to see its resolution, regardless of demographic and health-related factors. This study examines the effects of muscle mass enhancement, independent of exercise, on MASLD progression using myostatin knockout (Mstn-KO) mice, which are genetically modified to exhibit increased muscle mass due to myostatin deficiency.

Patients / Materials and Methods: 11-week-old Mstn-KO mice and their wild-type counterparts were fed a Western diet (WD) for 24 weeks to induce MASLD. Parameters assessed included liver steatosis through histological analysis, muscle mass via MRI and histological cross-sectional area, exercise performance through treadmill tests, and muscle strength measured by electrophysiology.

Results and Discussion: Mstn-KO mice showed significantly reduced liver steatosis (-20%) and increased muscle mass (+30%) compared to wild-type controls. Additionally, liver pro-inflammatory cytokines such as IL-1β and TNF-α were decreased in Mstn-KO mice, along with lower expression of lipogenesis-related genes, indicating a protective effect against MASLD progression. Histological assessments showed less hepatic lipid accumulation and inflammation in Mstn-KO mice, correlating with decreased myosteatosis and an enhanced cross-sectional area of muscle fibers. Muscle mass was measured by bioimpedance analysis, and paravertebral muscle area was evaluated using MRI. Electrophysiological measures indicated increased tetanic strength in Mstn-KO mice. Despite these physiological improvements, treadmill test results did not show significant differences in exercise performance between Mstn-KO and wild-type groups, suggesting that muscle mass improvement did not translate into enhanced exercise capacity. These results indicate that Mstn-KO mice are protected against muscle atrophy and MASLD progression.

Conclusions: Our findings suggest that increased muscle mass, independent of exercise performance, can significantly ameliorate MASLD histology. Mstn-KO mice serve as a valuable model for exploring muscle-liver crosstalk in liver diseases, indicating potential treatment pathways that do not rely on exercise enhancement.

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OP- 15 OUTCOME OF PREGNANCIES IN A SERIES OF WILSON DISEASE PATIENTS

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Conflict of interest: No

Introduction and Objectives: Wilson disease (WD) is an inherited disease that mainly affects the liver and brain due to copper overload. Pregnancy in WD is a challenging situation. Our aim was to analyze the clinical aspects and outcomes of pregnancies in WD.

Patients / Materials and Methods: In a series of 289 WD cases (1963-2024), we reviewed the medical records of 123 women, 26 of whom became pregnant at least once (1-5). A total of 52 pregnancies were recorded, but 3 were excluded because data on the conceptus were missing. Pregnancy outcomes were correlated with disease severity and anti-copper medication. Hepatic and/or neuropsychiatric manifestations were categorized as 1) asymptomatic/mild or 2) moderate/severe. Pregnancy outcomes were considered 1) successful

if the preterm/term infant survived the neonatal period or 2) unsuccessful if there was a miscarriage/fetal demise/perinatal death. Drug regimen during pregnancy were 1) penicillamine (DPA), 2) zinc (Zn) or 3) DPA/Zn if the patient had switched therapy for any reason. Statistical analysis was carried out using Fisher's test, with significance level at $p<0.05$.

Results and Discussion: Of the 49 pregnancies analyzed, 2 (4.1%) ended in maternal death and 17/49 (34.7%) in miscarriage/fetal or neonatal death. The Table below presents the results. The analysis of medication and pregnancy outcomes combined deteriorating and stable cases. There was a correlation between successful births and asymptomatic patients who had given birth before the onset of WD ($p<0.001$). In stable patients, successful births were slightly above significance ($p=0.062$). There was no significant difference among the outcomes in relation to the medication taken.

Conclusions: Pregnancy in symptomatic WD is potentially harmful to mother and conceptus. Successful births were significantly associated with pregnancies before the onset of WD symptoms, but were also possible with stable disease under treatment. Anti-copper drug regimen was not associated with pregnancy outcome.

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OP-16 FREQUENCY OF ATP7B GENE MUTATIONS IN A BRAZILIAN COHORT OF PATIENTS WITH WILSON'S DISEASE

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Conflict of interest: No

Introduction and Objectives: Wilson's disease (WD) is a rare genetic disease presenting more than 900 mutations in the ATP7B gene. The knowledge of the regional distribution of these mutations can improve the diagnosis of WD. We aimed to evaluate the frequency of ATP7B mutations in a WD Brazilian cohort and the association with disease phenotypes.

Patients / Materials and Methods: We performed molecular analysis by NGS of the 21 exons of ATP7B (Mendelics Genomic Analysis Laboratory) in patients with diagnosis of WD and in first-degree relatives undergoing WD investigation, followed in a single hepatology center. Demographic data and predominant type of WD presentation were assessed.

Results and Discussion: 28 patients were included (60% female; mean age 25 $\pm$ 13 years): 25 had an established diagnosis of WD and 3 were heterozygous relatives without disease. The phenotypes of WD were as follows: 15/25 (60%) with exclusively hepatic manifestation, 8/25 (32%) combination of hepatic and neurological, 1/25 (4.0%) isolated neurological manifestations and 1/25 (4.0%) were pre-symptomatic. We identified 17 ATP7B gene distinct mutations. The pathogenic variants c.3402delC, c.2123T>C and c.3818C>T presented the highest allele frequency, respectively, 25.5%, 15.7% and 15.7%. The majority (80.0%) presented the mutation in compound heterozygosity, 12.0% in homozygosity and 8.0% in simple heterozygosity. The c.2145C>T, c.1552T>C and c.3188C>T variants were considered of undetermined significance; c.2072G>T and c.3071_3072delTG variants were considered probably pathogenic. Regarding the disease phenotype, patients with mutations c.3402delC CG>C and c.2123T>C presented equal distribution of isolated hepatic or hepatic plus neurological phenotype, while c.3818C>T mutation was associated with predominantly hepatic phenotype. Presence of exon 2 deletion was associated with severe neurological manifestations.

Conclusions: The mutations c.3402delC, c.2123T>C and c.3818C>T were the most prevalent. The c.2145C>T and c.3188C>T variants, considered of undetermined significance, were found in confirmed cases of WD. An important heterogeneity of the ATP7B genotype associated with variation in phenotypic presentation was observed.

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P- 1 DEVELOPMENT OF LENTIVIRAL VECTORS FOR INHIBITION OF HEPATITIS B VIRUS, VIA SMALL INTERFERING RNA

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Conflict of interest: No

Introduction and Objectives: INTRODUCTION: Chronic hepatitis B represents a significant global health challenge. Current treatments often fail due to the persistence of HBV DNA as covalently closed circular DNA or integrated into the host genome, leading to viral reactivation. RNA interference (RNAi) emerges as a promising approach for treating chronic hepatitis through post-transcriptional gene silencing. OBJECTIVE: To design and evaluate the efficacy of RNAi lentiviral vectors targeting key HBV proteins (HBsAg, HBcAg, HBeAg) and pregenomic RNA (pgRNA) for silencing.

Patients / Materials and Methods: Silencing vectors were designed to target overlapping open reading frames, allowing simultaneous silencing of multiple viral proteins and pgRNA with a single RNAi construct. Three vector candidates (siHBV-1 to 3) underwent rigorous in silico testing to minimize off-target effects, evaluating stability and secondary structures. Lentiviral vector production was assessed using flow cytometry to detect green fluorescent protein expression in cell culture. Huh7 cells were transfected with 1 μg of purified HBV genotype A circular monomers, followed by infection