Background and aims: Survival into adulthood after palliative Fontan surgery for univentricular heart disease is increasing. Chronic hemodynamic changes can lead to multiorgan complications, including Fontan-associated liver disease (FALD) with risk of hepatocellular carcinoma (HCC) and hepatic decompensation. We report our experience in adult FALD patients (pts).
Method: All pts referred from Cardiology to our Liver Clinic since 2024 were included. Comorbidities screening followed EASL-ERN recommendations (*Téllez L. J Hepatol 2018*). Disease severity was classified by VAST score (1 point each for esophageal varices, ascites, splenomegaly, platelets < 150.000). Follow-up closed at 31/12/25.
Results: From 01/2024 to 12/2025, 24 FALD pts were evaluated. 20 pts (83.3%) underwent extracardiac and 4 (16.7%) intracardiac Fontan surgery in childhood (median age 6 years - y - [IQR 3.8–7]). At our first evaluation, median age was 29 y [26.5–37]; median time from Fontan surgery 23 y [18.8–25]; 70.8% male. NYHA class I in 15 pts (62.5%), II in 8 (33.3%), III in 1 (4.2%). 8 pts (33.3%) were on anticoagulants, 10 (41.7%) on pulmonary vasodilators and 10 (41.7%) on diuretics. Extrahepatic complications included 8 (33.3%) tachyarrhythmia, 3 (12.5%) sinus node dysfunction, 1 (4.2%) plastic bronchitis and 2 (8.3%) protein-losing enteropathy. 5 pts (20.8%) had implanted pacemakers, 4 pts (16.7%) experienced ischemic strokes, 3 peri-Fontan surgery or Fontan conduit replacement. VAST score was 0 in 6 pts (25%), 1 in 12 pts (50%), 2 in 5 pts (20.8%) and 4 in 1 pt (4.7%) with median time from Fontan surgery of 23.5 y [21.5–29.5], 23.5 y [22.8–25.3], 19 y [17–19] and 19 y, respectively. Notably, 5 pts (20.8%) had esophageal varices, 2 (13.6%) ascites, 8 (33.3%) splenomegaly and 11 (45.8%) thrombocytopenia. 21 pts (87.5%) underwent liver stiffness measurement (LSM), median of 20.9 kPa [16.0–26.4], without significant differences among VAST groups ($p = 0.53$, ANOVA test). 2 pts were referred due to HCC (Up-to-Seven in; AFP 1042 and 2.4 ng/mL at referral): both underwent combined heart-liver transplant (CHLT) after HCC downstaging and bridge therapy respectively. 1 pt had CHLT due to liver failure (NaMELD 24). The 3 transplanted pts are alive after 15 months, 13 days and 13 months respectively.
Conclusion: FALD is a major long-term complication in adult Fontan pts. Multidisciplinary follow-up is essential for early complication detection and timely CHLT referral. The role of LSM remains debated.

THU-305-YI

Dysregulation of hepcidin in hemochromatosis: results from a multinational cross-sectional study on serum iron parameters and MRI

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Background and aims: Hemochromatosis results from genetic dysregulation of the hepcidin–ferroportin axis, which precedes the development of overt iron overload. Homozygosity for p.Cys282Tyr in *HFE* is present in >80% of patients with hemochromatosis and UK Biobank data suggest a cumulative incidence of hemochromatosis of 56.4% in males and 40.5% in females by age 80. Elevated ferritin is a non-specific finding and is frequently observed in the context of inflammation or metabolic syndrome, limiting its diagnostic utility. The objective of this study was to assess markers of an inappropriately blunted hepcidin response in relation to serum iron parameters as well as liver and spleen iron concentrations to validate the concept that hemochromatosis is a state of hepcidin deficiency.
Method: Hepcidin, serum iron parameters and liver and spleen iron assessed by magnetic resonance imaging (MRI) were collected in a multinational cohort including 8406 individuals with *HFE* p.Cys282Tyr homozygosity and control participants with a normal *HFE* genotype and high ferritin in the majority in both groups.
Results: When patients were grouped by *HFE* genotype as p.Cys282Tyr homozygotes and controls, regression analysis of serum ferritin with hepcidin demonstrated a significantly shallower slope of the regression line in p.Cys282Tyr homozygous, consistent with an inappropriately low hepcidin response in this group. Ferritin and transferrin saturation (TSAT) showed log-linear correlations, with 20% higher TSAT values in p.Cys282Tyr homozygotes than in controls. Liver iron concentration (LIC), assessed by R2*-weighted MRI, was associated with ferritin in both groups; however, p.Cys282Tyr homozygotes exhibited higher LIC despite comparable ferritin values. Spleen iron was also related to systemic iron measures, but p.Cys282Tyr homozygotes consistently showed lower spleen iron, indicating relative iron sparing of the spleen.
Conclusion: This study confirms that the principal biochemical manifestation of hemochromatosis is elevated TSAT and a blunted hepcidin response to iron loading. Additional surrogates of this dysregulation include altered relationships between ferritin, liver iron and spleen iron. Based on these findings, phenotypic criteria supporting the diagnosis of hemochromatosis could include high TSAT, elevated liver iron and inappropriately low spleen iron and/or hepcidin.

THU-306-YI

Prevalence and risk factors of sarcopenia throughout the disease spectrum of symptomatic polycystic liver disease: a retrospective multicentre cohort study

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Background and aims: The severity of symptoms and complications such as malnutrition are key indications for volume-reducing therapy in patients with polycystic liver disease (PLD). Malnutrition is traditionally assessed by the mid-upper arm circumference (MUAC), although skeletal muscle index at the third lumbar vertebra (SMI-L3) is increasingly recognized as a more accurate marker of sarcopenia. This study aimed to determine the prevalence and clinical predictors of sarcopenia in patients with PLD, and assess whether sarcopenia predicts the need for volume-reducing therapy.
Method: This multicentre retrospective cohort study included 296 adult patients with symptomatic PLD. Sarcopenia was defined using SMI-L3 on CT: <39 cm^2/m^2 for females and <50 cm^2/m^2 for males. Reference values for MUAC were <23.1 cm for females and <23.8 cm for males. Additional variables included BMI, height-adjusted total liver volume (htLV), symptom severity (POLCA score), creatinine

levels and Charlson Comorbidity Index (CCI). Associations between sarcopenia and therapeutic needs were assessed using univariate tests and multivariable logistic regression adjusting for confounders (age, sex, BMI, ADPKD, malnutrition, POLCA score, htLV, creatinine levels and CCI).

Results: SMI-L3 was available for 137/296 (46.3%) patients of whom 80 (58.3%) had sarcopenia. Patients with and without sarcopenia showed no significant differences in MUAC value (39.4% vs 32.6%), POLCA score (22 ± 18 vs 20 ± 17), htLV (2667 ± 1675 mL vs 2539 ± 2048 mL) or CCI (2 ± 3 vs 3 ± 4); p-values all > 0.05. There was a significant difference in BMI (22 ± 4 vs 24 ± 5 kg/m^2, p = 0.009) and creatinine levels (1.01 ± 0.63 vs 1.14 ± 3.05 mg/dL, p = 0.040) among patients with and without sarcopenia respectively. In multivariable analysis only BMI (OR 0.81, p = 0.008) was an independent predictor for sarcopenia. The need for volume-reducing therapy was high (86.8%): somatostatin analogue (46.7%), resection/sclerotherapy (11.0%) and LTx (42.6%) (multiple treatments possible). After multivariable adjustment, sarcopenia independently predicted the need for volume-reducing therapy (OR 8.49, p = 0.018), alongside htLV (OR 1.001, p = 0.038) and CCI (OR 2.56, p = 0.033).

Conclusion: Sarcopenia is highly prevalent in patients with symptomatic PLD and predicts the need for volume-reducing therapy, whereas MUAC does not. Therefore, we recommend prioritizing sarcopenia measured by L3-SMI over MUAC in the management of PLD patients, especially in determining transplant eligibility.

THU-307

Genotype phenotype correlations and clinical presentation patterns in Wilson disease in a Sardinian cohort

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Background and aims: Wilson disease results from ATP7B mutations and presents with variable clinical expression. Sardinia shows a unique genetic profile dominated by the c.-436_-422del15 promoter deletion. This study aimed to evaluate genotype-phenotype associations, age at onset and clinical presentation patterns in a large Sardinian cohort.

Method: We retrospectively analyzed 118 patients with Wilson disease (Leipzig score >=4) followed between 1978 and 2024. Clinical, biochemical, neurological, radiological and genetic data were collected. Liver fibrosis was assessed using Metavir. Patients were classified by genotype, phenotype (hepatic or neurological) and outcome (alive, transplanted, deceased). Statistical analyses included chi-square, t-test and ANOVA ($p < 0.05$).

Results: The Sardinian promoter deletion accounted for 89.5% of genotypes and was strongly associated with a hepatic phenotype (84%) and lower aspartate aminotransferase and alanine aminotransferase values compared with non-Sardinian genotypes. Variants p.V1146M and p.R778W showed higher neurological involvement (52% and 67%). The mean age at diagnosis was 24.5 years, with 76% diagnosed <=35 years. Early diagnosis correlated with milder fibrosis ($p = 0.02$). Patients alive at last follow-up were diagnosed significantly earlier than transplanted or deceased patients ($p = 0.003$). Histology showed milder fibrosis in the promoter deletion, while non-Sardinian genotypes exhibited more advanced staging.

Conclusion: The Sardinian promoter deletion is associated with hepatic involvement, lower necro-inflammatory activity and a more favorable clinical course. Non-Sardinian genotypes display a higher neurological burden and more severe fibrosis. Early diagnosis remains a key determinant of outcome, supporting targeted screening in genetically enriched regions.

THU-308

Characteristics of the adolescent population with Alagille syndrome and their liver survival

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