(NAFLD-HCC). We aimed to assess the natural history and epidemiology of all patients with NAFLD-HCC between 1990 and 2014 in a well-defined population.
Method: All HCC cases resident in the canton of Geneva, Switzerland, diagnosed between 1990–2014 were identified from the prospective Geneva cancer registry and all data was manually checked and completed using Geneva university hospital electronic health records. NAFLD-HCC was diagnosed when specifically stated or when other causes of liver disease were excluded in the presence of type 2 diabetes, metabolic syndrome or obesity.
Results: 920 patients were diagnosed with HCC in the canton of Geneva between 1990–2014. Major aetiologies of underlying liver disease were alcohol (43.2%), hepatitis C and B viruses (20.7% and 9.1% respectively), and NAFLD (8.3%). The 76 NAFLD-HCC subjects were significantly older, had higher rates of obesity (46.6% vs 13.4%, $p < 0.001$), diabetes (73.0% vs 39.6%, $p < 0.001$) and were more commonly female (31.6% vs 18.6%, $p = 0.006$). The age-standardized incidence (ASI) of HCC increased between 1990–94 to 2010–14 from 11.6 to 12.8/100,000 in men and 1.8 to 3.3/100,000 in women. The proportion of NAFLD-HCC increased significantly in both sexes, but in particular in women from 0% in 1990–94 to 30% in 2010–14 (Figure).

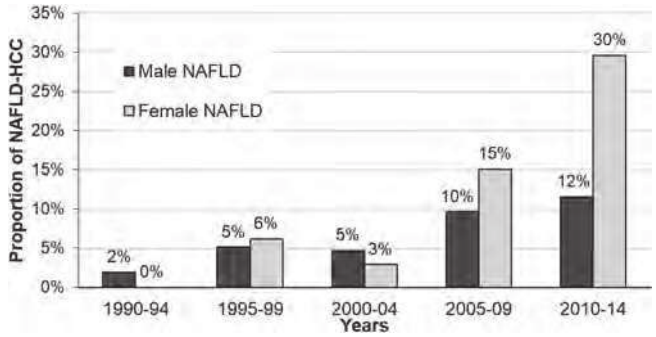

Figure: Proportion of NAFLD-HCC by sex between 1990–2014.

Conclusion: In a prospective populational cohort of HCC subjects spanning 24 years, NAFLD-HCC accounted for 8% of all HCCs. Compared to non-NAFLD-HCC, NAFLD-HCC patients were older, more comorbid and more frequently female. NAFLD is a rising cause of HCC, in particular in women. This study underlines the specific clinical characteristics of NAFLD-HCC, which will help to guide future recommendations and research.

THU041

Muscle fat infiltration in obese patients is associated with NAFLD related fibrosis severity - results from a prospective imaging study

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Background and Aims: The association between NAFLD and visceral adipose tissue or sarcopenia has been reported, although results are discordant. The goal of this study is to analyze the spectrum of NAFLD among obese patients recruited prospectively and to detect clinical, biological and imaging data associated with steatosis or fibrosis.
Method: Baseline data of obese patients (BMI ≥ 30) randomized in a single center (Food4Gut study) were recorded. Transient elastography (TE) was done to quantify both liver steatosis by controlled attenuation parameter (CAP) measurement and liver fibrosis by liver stiffness measurement (LSM). Body composition was evaluated using bioelectrical impedance analysis. Subcutaneous adipose tissue (SAT), visceral adipose tissue (VAT), muscle areas and muscle fat infiltration (MFI) were measured on CT-scan images at the third lumbar level.
Results: Fifty-two Caucasian patients (mean age: 50 years, 50% male, mean BMI 35.8) were included. TE was successful in 49 patients (94%). XL probe was used in 20 patients (38%). Mean LSM was low (6.5 kPa). Mean CAP result was high (324 dB/m) with the majority of the patients (73%) presenting severe steatosis (CAP ≥ 296 dB/m). 12 patients (24%) had advanced fibrosis defined by LSM ≥ 7.8 kPa (M probe) or ≥ 6.4 kPa (XL probe). Factors associated with severe steatosis and advanced fibrosis are summarized in the table. Interestingly, severe steatosis was associated with higher muscle quantity and severe fibrosis with a lower muscle density index, compatible with MFI. In a multivariate logistic regression analysis, MFI index was the strongest predictor of advanced liver fibrosis.
Conclusion: In summary, among obese patients, a high proportion of severe steatosis was diagnosed and advanced liver fibrosis was suspected in 24% of the patients. MFI provides a robust, skeletal muscle-specific characteristic linked to advanced fibrosis in NAFLD,

Table: (abstract: THU041)

	Parameter	Light-moderate steatosis	Severe steatosis	p-value	No fibrosis	Advanced fibrosis	p-value
Clinical parameters	Age (years)	49.2	50.1	NS	49.8	50.0	NS
	Weight (kg)	97.5	108.1	0.035	101.0	119.2	0.0035
	BMI (kg/m²)	34.3	36.5	NS	34.8	39.2	0.059
	Waist (cm)	112.0	116.9	NS	112.7	124.6	0.027
Biological results	ALAT (UI/L)	28.1	45.3	0.0059	35.4	57.2	NS
	γGT (UI/L)	40.0	50.6	NS	45.4	55.8	NS
	Fasting glycemia (mg/dL)	95.1	109.2	0.013	106.4	103.1	NS
Bioimpedance analysis	R	479.9	438.9	NS	460.7	417.1	0.048
	Fat free mass (kg)	61.7	68.6	NS	63.9	76.3	0.0034
	Total body fat (kg)	37.8	39.4	NS	38.0	42.9	NS
CT scan data	Subcutaneous fat area (cm²)	340.4	363.1	NS	338.8	413.6	NS
	Visceral fat area (cm²)	197.3	275.4	0.0066	236.6	310.2	0.054
	Whole muscle area (cm²)	153.2	182.7	0.038	166.4	200.1	0.0086
	Skeletal muscle index (cm²/m²)	52.9	61.9	0.028	57.6	65.1	0.054
	Whole muscle density index (UH/cm²)	0.208	0.185	NS	0.200	0.163	0.0051

suggesting a muscle-liver axis in the pathogenesis of NAFLD complications.

THU042

Exercise performance in patients with non-alcoholic steatohepatitis

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Background and Aims: Prior studies indicate that those with nonalcoholic fatty liver disease (NAFLD) have poorer exercise capacity compared to age-matched controls. Moreover, cross-sectional data in those with NAFLD suggest an inverse correlation between disease severity and self-reported exercise intensity. The underlying contributors of poor exercise capacity in patients with NAFLD is unclear. Our aim was to evaluate exercise performance in patients with biopsy-proven nonalcoholic steatohepatitis (NASH).
Method: Patients with biopsy-proven NASH (n = 10), graded and staged according to the NASH Clinical Research Network grading and staging system, and controls (n = 11), those without a diagnosis of biopsy-proven NAFLD were recruited. Participants performed 10-intervals of vigorous-intensity interval training (30 seconds exercise, 60 seconds rest) on a Concept2 indoor rowing machine at 80–90% of predicted maximum heart rate (220-Age). Intensity was recorded after each interval using the BORG scale of perceived exertion. Age, BMI, distance, power output, and $BORG_{peak}$ were compared between groups using Exact-Wilcoxon rank sum test or Fisher's exact test. Generalized linear modeling was used to adjust for age, gender, and BMI.
Results: Mean ages of participants were 51.0 ± 14.9 in the NASH group and 42.4 ± 13.6 in controls, $p > 0.05$. BMI was higher in the NASH group (32.5 ± 3.3) compared to controls (26.6 ± 4.6). Mean power output (watts) over the 10 exercise intervals was significantly lower in the NASH group (103.6 ± 30.4) compared to controls (231.0 ± 140.4), $p < 0.01$. Total distance rowed (meters) after 10-intervals was also lower in the NASH group (987.2 ± 115.7) compared to controls (1266.6 ± 259.4), $p < 0.01$. $BORG_{peak}$ was lower in the NASH group (14 ± 1) compared to controls (17 ± 2), $p < 0.01$. After adjusting for age, gender, and BMI the difference in mean power output, total distance, and $BORG_{peak}$ all remained significant, $p < 0.01$.
Conclusion: Compared to controls, those with NASH have lower exercise power output, rowing distance, and perceived exercise intensity. Failure to reach perceived exercise intensity beyond steady state (BORG ≥ 17) may serve as a potential biomarker for poor metabolic function as well as an underlying contributor of poor exercise performance in those with NASH.

THU044

Obesity and alcohol intake modify the impact of genetic variants on the risk for incident liver disease in the general population

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Background and Aims: Genetic variants and modifiable lifestyle factors including abdominal obesity and alcohol intake are risk factors for liver disease. We studied the interaction between genetic variants, abdominal obesity and alcohol intake for incident advanced liver disease (ILD).
Method: Our study included 32,942 persons (mean age 50 yrs, 47% men) who participated in health-examination surveys (FINRISK1992–2012 or Health 2000) with available data on alcohol intake (median 26.0 g/wk), waist-hip ratio (WHR, mean 0.89) and genotypes associated with liver disease in PNPLA3, TM6SF2, MBOAT7, SERPINA1 and HFE. A genetic risk score (GRS) was calculated as the sum of these risk alleles. Data were linked with national health registers for liver-related outcomes (hospitalizations, malignancies, and death). Exclusions were baseline clinical liver disease or viral hepatitis. Analyses were adjusted for age, WHR and alcohol intake.
Results: TM6SF2 rs58542926 ($p < 0.05$) and SERPINA1 rs28929474 ($p < 0.02$) genotypes interacted significantly with WHR. Among carriers of these risk variants, the cumulative incidence of liver disease was significantly higher than non-carriers when WHR exceeded ~1.0, but not below WHR 1.0. The GRS showed a dose-

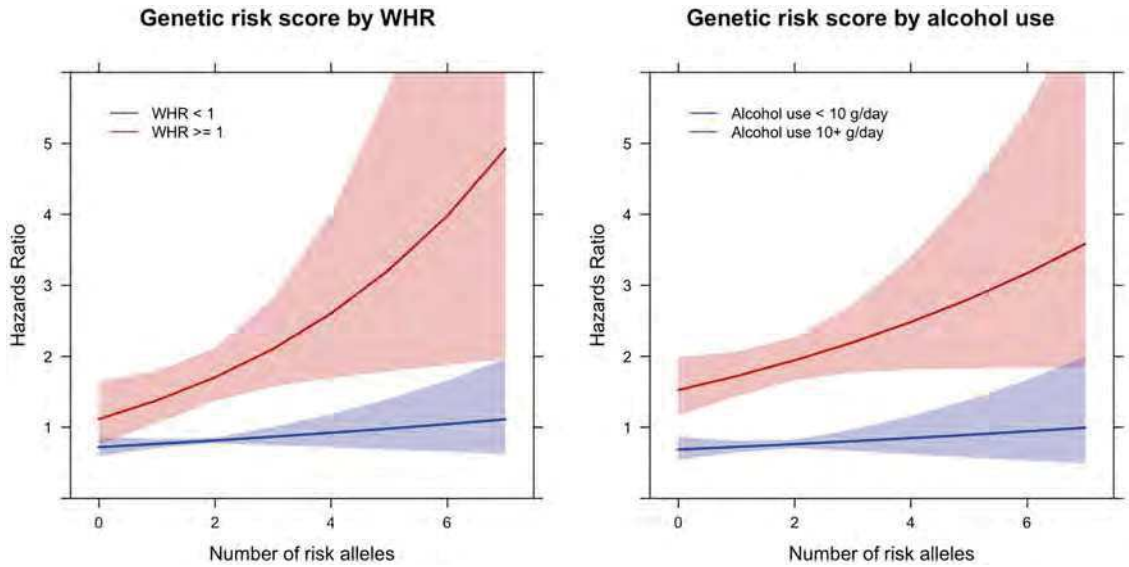

Figure: (abstract: THU044)