ELSE KRÖNER-FORSCHUNGSKOLLEG MAINZ

Higher scores in the Clinical Frailty Scale are associated with covert and overt hepatic encephalopathy in patients with cirrhosis

E. M. Schleicher, MD[1,2], L. Kaps, MD, PhD[1,2], J. M. Schattenberg, MD[1,2], P. R. Galle, MD[1,2], M.- A. Wörns, MD[3], S. J. Gairing,MD[1,2], C. Labenz, MD[1,2]

1 Department of Internal Medicine I, University Medical Center of the Johannes Gutenberg-University, Mainz, Germany
2 Cirrhosis Center Mainz (CCM), University Medical Center of the Johannes Gutenberg-University, Mainz, Germany
3 Clinic for Gastroenterology, Hepatology and Endocrinology, Hannover Medical School, Hannover, Germany

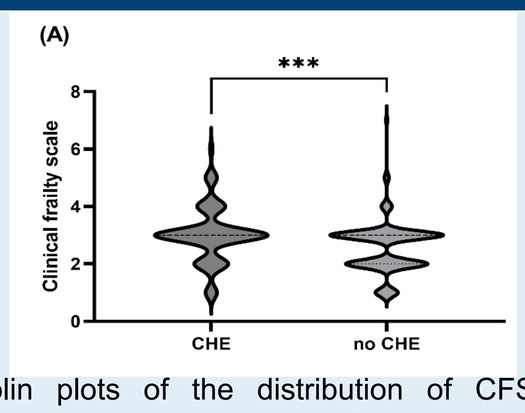
Background & Aims

- Hepatic encephalopathy (HE) represents one of the most severe complications of cirrhosis. The occurrence of overt HE (OHE) and even the presence of covert HE (CHE) can be seen as an indicator of poorer prognosis and heavily affect patients' well-being[1,2].
- Frailty is common in patients with liver cirrhosis and increases the vulnerability to internal and external stressors[3,4].
- **This study aimed to investigate the impact of frailty, as defined by the validated Clinical Frailty Scale (CFS), on the risk of CHE and OHE development in patients with cirrhosis**

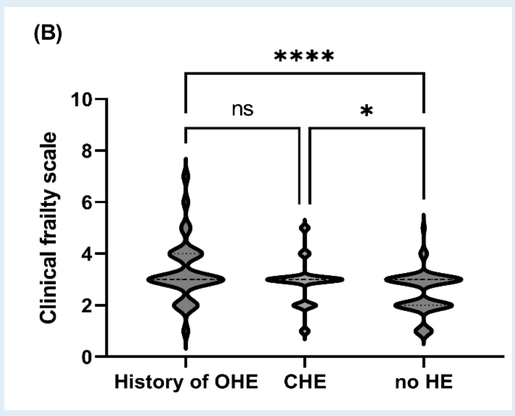
Patients & Methods

- 228 out- or electively hospitalized patients with cirrhosis recruited at the Cirrhosis Center Mainz, Germany
- Frailty was assessed using the CFS
- Patients were examined for the presence of CHE at study inclusion using the West-Haven-Criteria (HE1) and the psychometric hepatic encephalopathy score (PHES)
- All patients were followed for the development of OHE

Results

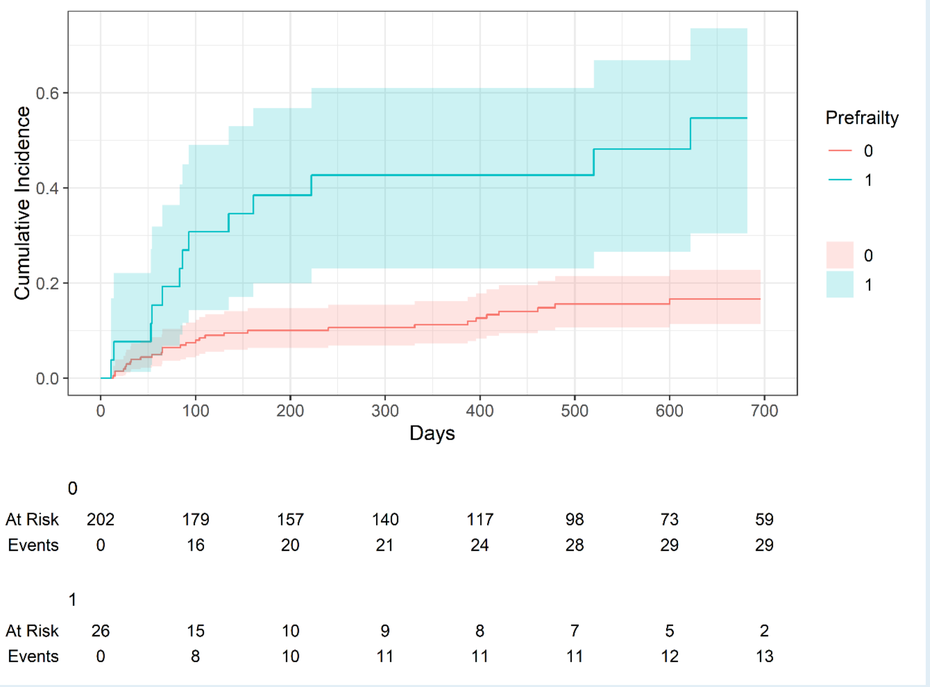


Violin plots of the distribution of CFS in patients with and without CHE (*** p < 0.001).



Violin plots of the distribution of CFS in patients with a history of OHE, patients with CHE but no history of OHE and patients without HE (* p < 0.05, **** p < 0.0001

Variable		All patients n = 228	Patients with CHE n = 71	Patients without CHE n = 157	p-value
Age, y (IQR)		60 (53; 66)	62 (54; 69)	59 (53; 65)	0.209
Male gender, n (%)		129 (56.6)	46 (64.8)	83 (52.9)	0.093
Aetiology	**Alcohol, n (%)**	74 (32.5)	30 (42.3)	44 (28.0)	0.172
	Viral hepatitis, n (%)	45 (19.7)	12 (16.9)	33 (21.0)	
	NAFLD, n (%)	29 (12.7)	9 (12.7)	20 (12.7)	
	Cholestatic/ Autoimmune, n (%)	31 (13.6)	5 (7.0)	26 (16.6)	
	Other/mixed, n (%)	49 (21.5)	15 (21.1)	34 (21.7)	
Median MELD score (IQR)		10 (8; 14)	13 (8; 17)	10 (7; 13)	**<0.001**
Child-Pugh A/B/C, n (%)		138/69/21 (60.5/30.3/9.2)	26/31/14 (36.6/43.7/19.7)	112/38/7 (71.3/24.2/4.5)	**<0.001**
History of ascites, n (%)		117 (51.3)	45 (63.4)	72 (45.9)	0.014
History of OHE, n (%)		33 (14.5)	22 (31.0)	11 (7.0)	**<0.001**
Sodium, mmol/l (IQR)		139 (137; 140)	138 (135; 140)	139 (137; 140)	0.088
Albumin, g/l (IQR)		34 (29; 38)	30 (25; 37)	35 (31; 38)	**<0.001**
CHE, n (%)		71 (31.1)	71 (100)	0 (0)	N/A
CFS (IQR)		3 (2; 3)	3 (3; 3)	3 (2; 3)	**<0.001**



Cumulative overt hepatic encephalopathy incidences for patients with and without pre-frailty (CFS > 3 vs. CFS ≤ 3, p < 0.001).

Variables associated with the development of overt hepatic encephalopathy in the subcohort of patients without a history of OHE (n = 195)

	Multivariable Cox regression analysis Model 1		Multivariable regression analysis using the Fine and Gray method Model 2	
	HR (95% CI)	p-value	sHR (95% CI)	p-value
MELD score	1.071 (1.000 – 1.147)	**<0.001**		
Albumin	0.824 (0.757 – 0.897)	**<0.001**	0.85 (0.78 – 0.93)	**<0.001**
CFS	1.817 (1.171 – 2.818)	**0.008**	1.88 (1.18 – 2.99)	**0.008**

Model 1: The multivariable Cox regression model was performed with a stepwise variable selection procedure. Not significant were: CHE (p = 0.064), sodium (p = 0.273) and history of ascites (p = 0.637).

Model 2: The multivariable regression analysis using the Fine and Gray method was performed with a predefined inclusion variable selection. Not significant were: CHE (p = 0.2), sodium (p = 0.5), history of ascites (p = 0.6) and MELD (p = 0.4).

Conclusion

- **Poorer physical functioning, quantified by CFS, is associated with the presence of CHE in patients without a history of OHE.**
- **A higher CFS is strongly associated with OHE development irrespective of the presence of CHE at baseline.**
- **CFS may serve as an easy and inexpensive tool to identify patients at higher risk of HE in clinical routine.**
- **The results highlight the need for preventive measures such as adequate nutrition and medical exercise therapy.**

Acknowledgements: Dr. E.M. Schleicher is supported by the Clinician Scientist Fellowship "Else Kröner Research College: 2022_EKFK.05".

Dr. Eva M. Schleicher
Department of Internal Medicine I, University Medical Center of the Johannes Gutenberg-University, Mainz, Germany
Mail: eva.schleicher@unimedizin-mainz.de; Twitter: @EvSchleicher

Else Kröner Fresenius Stiftung
TRANSMED Mainz Research School of Translational Biomedicine
JG|U UNIVERSITÄTSmedizin. MAINZ