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Value of six minimal hepatic encephalopathy tests in predicting clinical outcome in patients with liver cirrhosis

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Introduction

- The development of overt hepatic encephalopathy (oHE) is an important complication in patients with liver cirrhosis.
- HE is associated with increased risk of rehospitalization and mortality.
- Proper estimation of the individual risk of developing oHE, rehospitalization and death for any patient would help to improve patient-centered care.
- We evaluated six widely used mHE tests in respect of their predictive value for oHE, rehospitalization and death.

Materials & Methods

- 132 patients with liver cirrhosis were prospectively recruited (**Figure 1**).
- mHE assessment consisted of PSE-Syndrome Test (PHES), Animal Naming Test (ANT), Critical Flicker Frequency (CFF), Inhibitory Control Test (ICT), EncephalApp (Stroop) and Continuous Reaction Time Test (CRT).
- Patients were monitored for 365 days regarding development of oHE, rehospitalization and death (**Figure 2**).
- We performed competing risk analyses (treating death/liver transplantation as competitor) for oHE and rehospitalization and cox regression for death. In the multivariable model, we adjusted for CHE, previous oHE and Child-Pugh-Score.

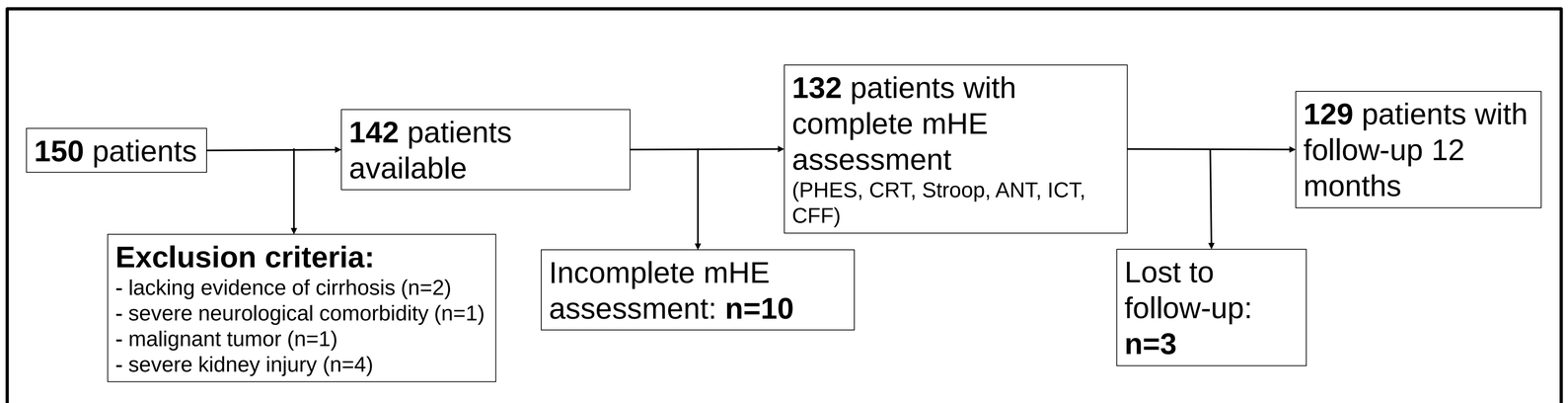

Figure 1: Study design

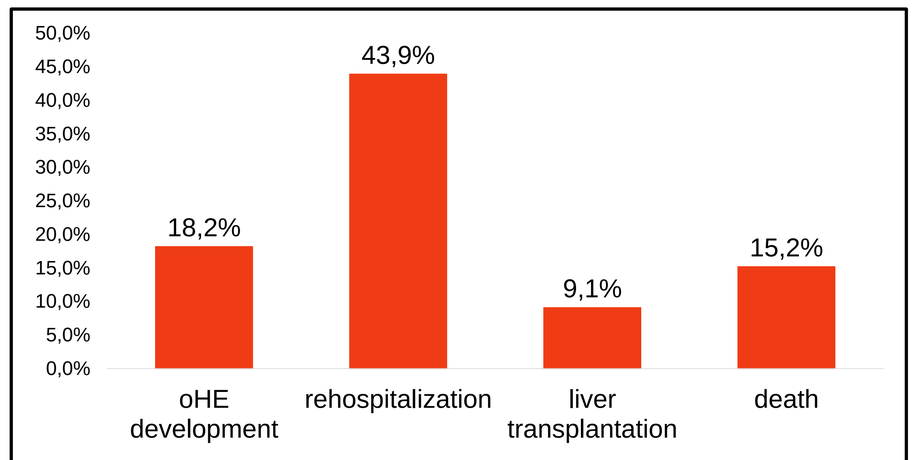

Figure 2: Events of interest during follow-up 365 days

Results

Baseline characteristics	N=132
Age	57 (51-65)
Sex female	41 (31.1%)
Child-Pugh-Score	7 (6-9)
MELD	11 (9-15)
TIPS	36 (27.3%)
Diabetes	35 (26.5%)
Previous oHE episodes	40 (30.3%)
Etiology	
ALD	47 (35.6%)
MASLD	21 (15.9%)
MetALD	13 (9.8%)
Viral	14 (10.6%)
PSC, PBC, AIH	17 (12.9%)
Other etiology	20 (15.2%)
mHE test results	
PHES	-4 (-8- -2)
PHES abnormal	62 (47%)
CRT Index	1.861 (1.4305-2.316)
CRT abnormal	67 (50.8%)
Stroop Off+OnTime (sec)	188.7 (162.8-218.7)
Stroop abnormal	79 (59.8%)
ANT (animals/minute)	21 (17-27)
ANT abnormal	77 (58.3%)
ICT weighted lures	18.6 (8.8-38.7)
ICT abnormal	58 (43.9%)
CFF (corrected for SD)	41.55 (38.62-46.22)
CFF abnormal	37 (28%)
Lab values	
Sodium (mmol/l)	136 (134-139)
Creatinine (µmol/l)	86 (70-110)
CHE (kU/l)	3.15 (2.13-4.47)
Bilirubin (µmol/l)	25 (15-45)
Albumin (g/l)	33 (28-37)
White blood cells (tsd/µl)	4.85 (3.73-7.38)
Platelets (tsd/µl)	99 (62-139)
Hemoglobin (g/dl)	11.1 (9.8-13.0)
INR	1.24 (1.11-1.37)
HE prophylaxis intake	
Lactulose intake	70 (53%)
Rifaximin intake	46 (34.8%)
L-Ornithine L-Aspartate intake	21 (15.9%)

Table 1: Baseline characteristics

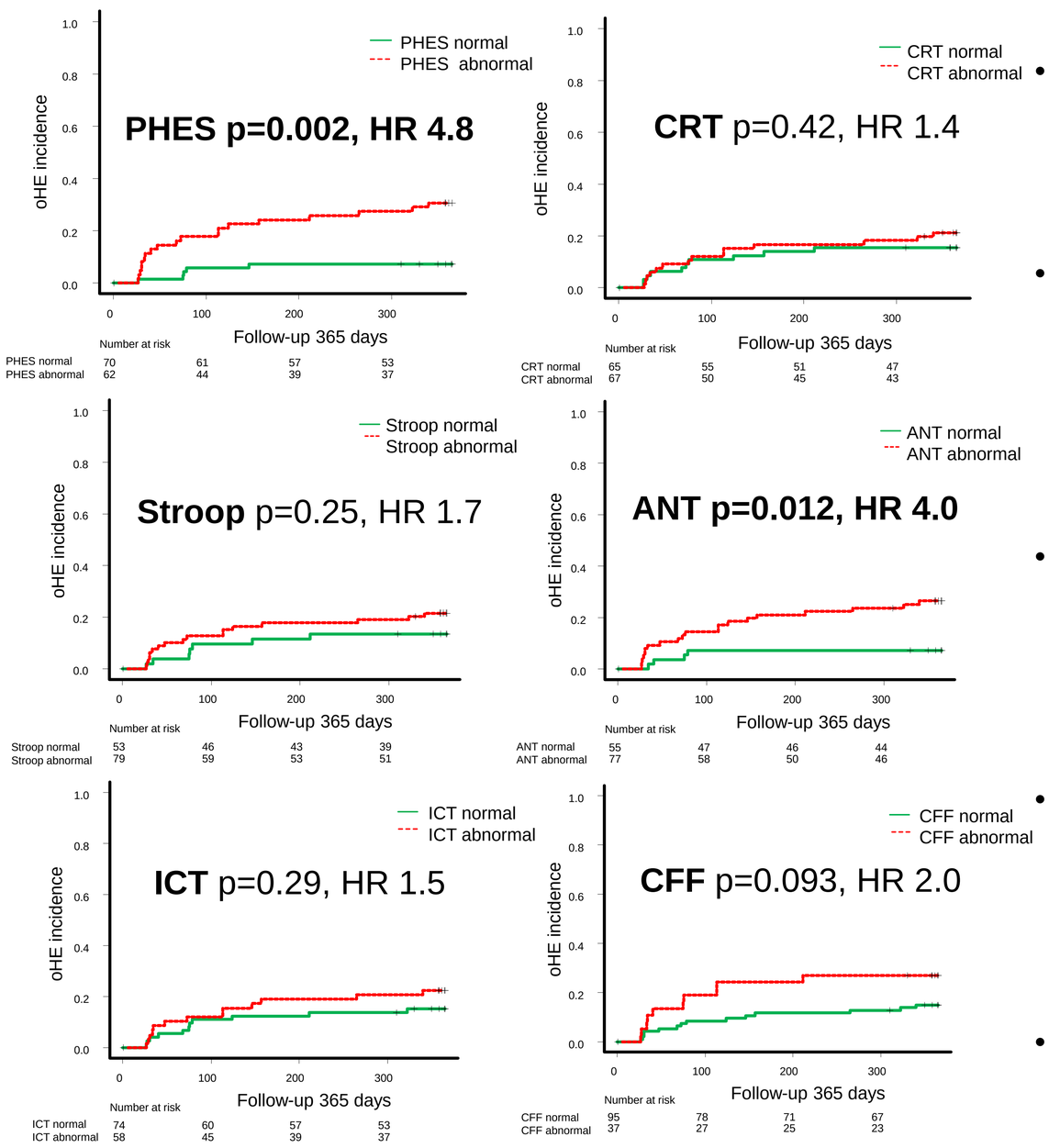

Figure 3: Univariable competing risk analyses for oHE development

- At baseline, median age was 57, median MELD 12 and Child Pugh Score 7 (**Table 1**).
- During follow-up, 24 (18%) patients developed oHE, 58 (44%) were re-admitted to hospital and 32 (24%) patients died or underwent liver transplantation.
- Abnormal PHES and ANT were significantly linked to oHE development during follow-up in competing risk analyses (**Figure 3**). In the multivariable model, only PHES remained significantly associated to oHE development.
- Regarding rehospitalization, only abnormal PHES results showed a significant correlation. None of the tests were significantly linked to rehospitalization in the multivariable model.
- Abnormal uncorrected ANT results (<23 animals) were significantly associated with mortality in cox regression (HR: 2.397; p=0.032). ANT was significantly associated in the multivariable model.
- Abnormal results in CRT, ICT, Stroop or CFF were not significantly linked to any clinical endpoint (development of oHE, rehospitalization, death).

Conclusion

- This study underlines the frequency of poor outcome in patients with cirrhosis and mHE.
- PHES was the most reliable among the mHE tests in predicting oHE.

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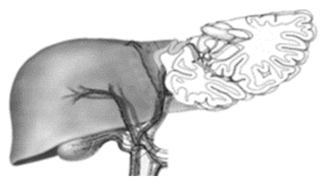

GHE Gastroenterology Hepatology Infectious Diseases Endocrinology

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