

Hepatic encephalopathy is associated with a poorer long-term prognosis than non-hepatic encephalopathy in cirrhotic patients

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Introduction

- Survival dramatically decreases after a first episode of clinical **hepatic encephalopathy (HE)**
- Hyperammonemia, both isolated and in the context of HE, is associated with poorer prognosis at short and long term.
- Some patients display clinical encephalopathy without hyperammonemia, defined as **non-hepatic encephalopathy (nHE)**
- No studies have compared the prognosis of HE with that of nHE.**

Materials and methods

- Retrospective observational study**
- Two different cohorts** of patients hospitalized in Liver Intensive Care Unit between February 2014 and October 2016, and between January 2019 and August 2021.
- All patients had at least one **measurement of blood ammonia (NH3) on admission.**
- Hyperammonemia (hNH3) was defined by **blood ammonia > 50 µmol/L.**

Results

- 533 patients included**, divided into 4 groups

With encephalopathy

- Gp 1: Overt hepatic encephalopathy (OHE)**, 169 pts
- Gp 2: Non-hepatic encephalopathy (nHE)**, 77 pts

Without encephalopathy

- Gp 3: normal ammonia (noE/nNH3)**, 126 pts
- Gp 4: hyperammonemia (noE/hNH3)**, 161 pts

- Patients with HE have more history of chronic renal failure than patients with nHE (Table 1).
- Patients with nHE are **more exposed to encephalopathy-providing drugs** than patients with HE (Table 1) and patients without encephalopathy and without hyperammonemia (Table 2).
- Presence of an **infection at admission** is associated with the presence of nHE (Table 2).
- Significantly lower one-year transplant-free survival in patients with hepatic encephalopathy** (Figures 1 and 2) compared to those with nHE and those without clinical encephalopathy.

Conclusion

- nHE** – ie encephalopathy without hNH3 – is common in cirrhotic patients with encephalopathy, and is probably of **drug-induced or septic origin.**
- The prognosis of nHE is not different from that of patients without encephalopathy.
- HE, but not nHE, is independently associated with poorer transplant-free survival in cirrhotic patients admitted to liver-ICU.**
- The presence of chronic renal failure could partly explain this result by favoring hyperammonemia.

Table 1. Comparison of patients with HE (group 1) versus those with nHE (group 2)

	Group 1 OHE N=169	Group 2 nHE N=77	p-value
Chronic renal failure, n (%)	17 (10.1)	2 (2.6)	0.042
Cirrhosis of alcoholic origin, n (%)	121 (71.6)	66 (85.7)	0.016
MELD score, median [IQR]	22 [16 - 29]	22 [18 - 30]	0.257
Exposure to beta-lactams at admission, n (%)	34 (20.1)	27 (35.1)	0.017

Table 2. Factors associated with the presence of nHE

	Group 2 nHE N=77	Group 3 noE/nNH3 N=126	p-value
Cirrhosis of alcoholic origin, n (%)	66 (85.7)	78 (61.9)	< 0.001
Presence of an infection at admission, n (%)	54 (70.1)	40 (31.7)	< 0.001
MELD score, median [IQR]	22 [18 - 30]	19 [11 - 23]	< 0.001
CLIF-C OF score, median [IQR]	9 [8 - 10]	7 [6 - 8]	< 0.001
Exposure to beta-lactams at admission, n (%)	27 (35.1)	23 (18.3)	0.011
Exposition to efflux pump inhibitors, n (%)	42 (54.5)	49 (38.9)	0.041

Figure 1. Adjusted survival curve representing the probability of death and/or liver transplantation at 1 year according to the presence or absence of encephalopathy and the presence or absence of hyperammonemia

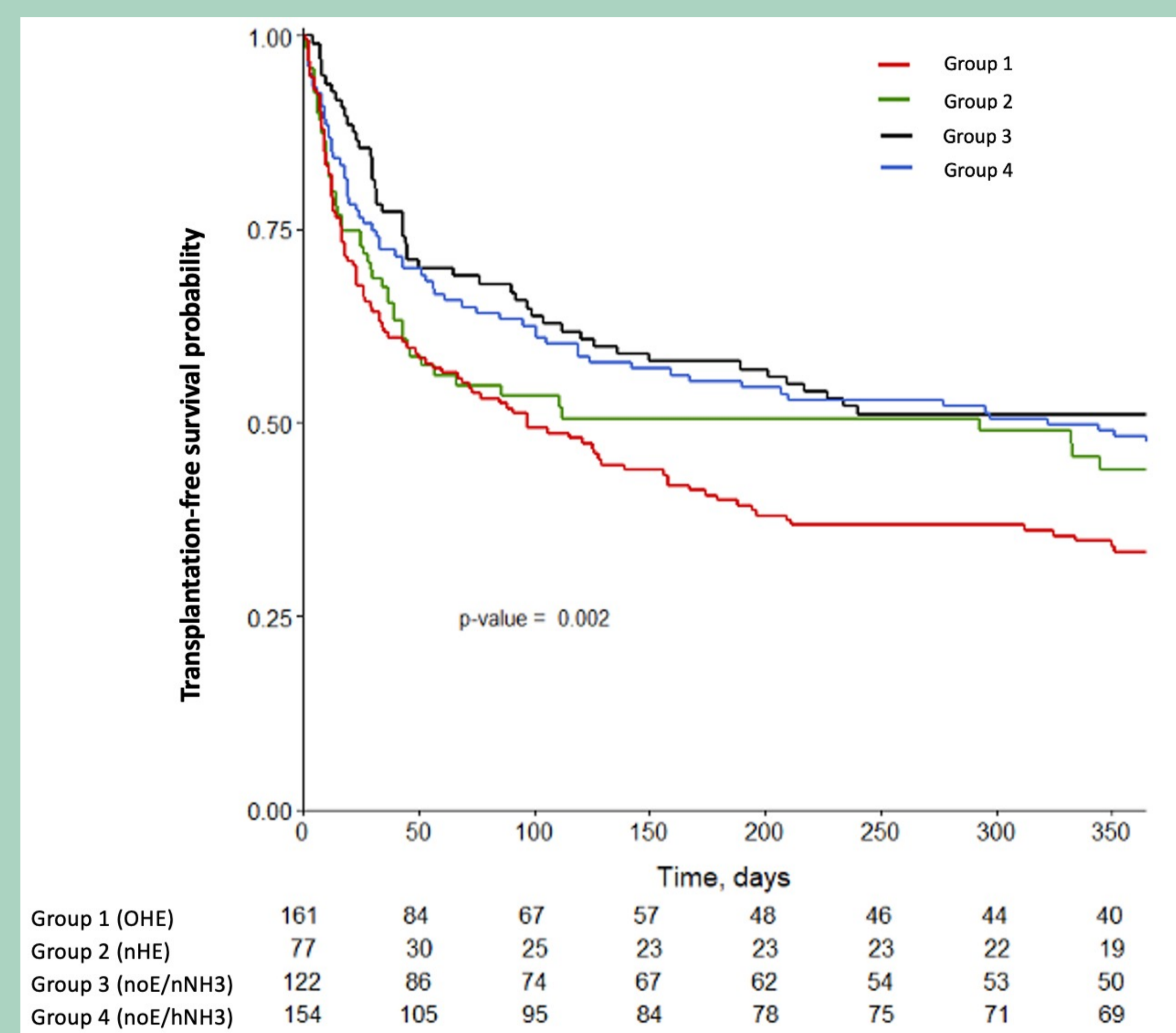


Figure 2. Forrest plot representing the hazard-ratios, with their confidence intervals and their p-value, of the factors associated or not with lower one-year transplant free survival after multivariate analysis

