

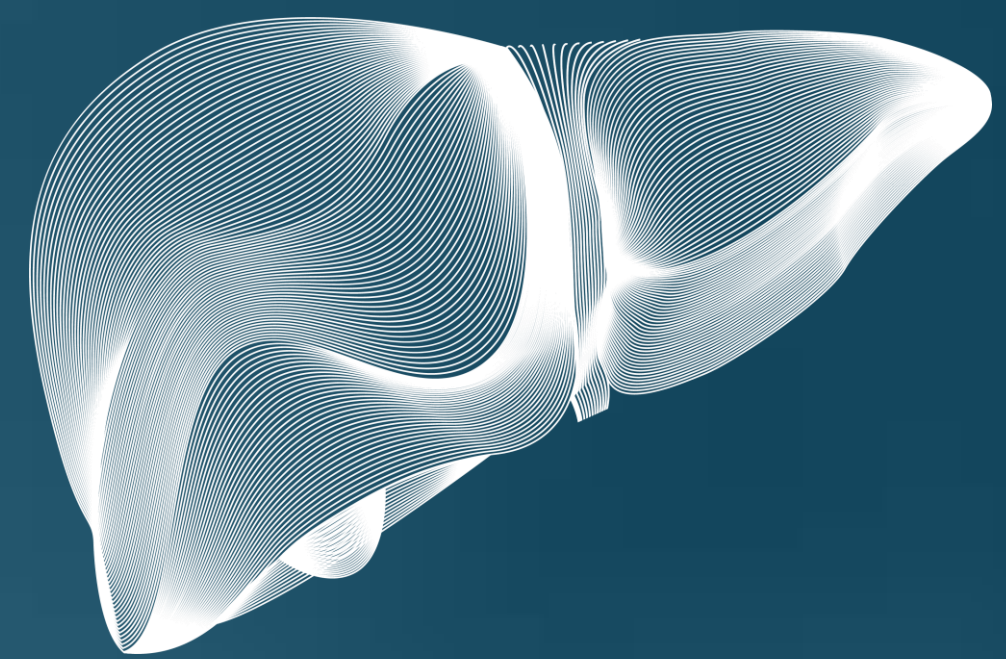
A composite score of PRO-C6 and platelet count is prognostic for liver-related outcomes in patients with chronic hepatitis C

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BACKGROUND

- There is a need to identify prognostic markers for patients with chronic liver disease at increased risk of developing a liver-related outcome.
- Endotrophin, a signal peptide that is a driver of fibroblast activation and promotion of fibroinflammatory disease, can be assessed using the nordicPRO-C6TM assay.
- PRO-C6 is elevated in several fibroinflammatory diseases
- We have previously shown the prognostic value of PRO-C6 for identifying patients with chronic hepatitis C (CHC) cirrhosis at higher risk of developing a liver-related outcome

Our aim was to explore the diagnostic utility of a composite score of PRO-C6/Platelets to predict liver-related outcomes in The Hepatitis C Antiviral Long-Term Treatment Against Cirrhosis Trial (HALT-C) (ClinicalTrials.gov #NCT00006164).

METHODS

- Our study population included 339 chronic hepatitis C (CHC) patients with and without cirrhosis from the HALT-C cohort
- NordicPRO-C6TM was measured in serum from baseline, using a fully validated competitive enzyme-linked immunosorbent assay from The FIB-NIT PanelTM.
- **A composite score of baseline PRO-C6/Platelet count was calculated**
- **Patients were dichotomized into above and below 0.0968 derived from upper quartile PRO-C6 = 15 ng/mL / median Platelet count = 155 x 10³/μL**
- Liver-related events included death, Child- Pugh score ≥7, variceal hemorrhage, ascites, bacterial peritonitis, encephalopathy, and hepatocellular carcinoma.
- Kaplan-Meier estimates and Cox regression were used to evaluate the prognostic value of PRO-C6/Platelet count to identify patients at higher risk of developing liver-related events.
- Data provided by NIDDK CR, a program of the National Institute of Diabetes and Digestive and Kidney Diseases.

RESULTS

Demographics

Table 1.	All patients N = 339 ¹	No cirrhosis N = 188 ¹	Cirrhosis N = 151 ¹	p-value ²
Baseline Characteristics				
Gender, female	109 (32%)	62 (33%)	47 (31%)	0.7
Age, years	50 (47, 55)	50 (47, 54)	50 (47, 55)	>0.9
BMI, kg/m ²	29.4 (26.6, 32.6)	29.5 (26.4, 32.6)	29.3 (26.7, 32.6)	>0.9
Alcohol consumption, drinks/week	4 (0.7, 12.6)	3.5 (0.5, 10.4)	4.6 (0.8, 14.2)	0.2
ALT, U/L	87 (61, 129)	86 (57, 124)	90 (65, 133)	0.3
AST, U/L	73 (53, 101)	68 (49, 95)	82 (60, 114)	0.001
Platelet count, x10 ³ /μL	155 (116, 204)	175 (134, 221)	133 (92, 175)	<0.001
PRO-C6, ng/mL	12.4 (10.0, 15.0)	11.5 (9.6, 14.2)	13.3 (10.7, 17.2)	<0.001
Ishak fibrosis score 2/3-4/5-6, n	21/167/151	21/167/0	0/0/151	<0.001
Liver-related event	66 (19%)	19 (10%)	47 (31%)	<0.001

¹ n (%); Median (IQR), ²Pearson's Chi-squared test; Mann-Whitney U test.

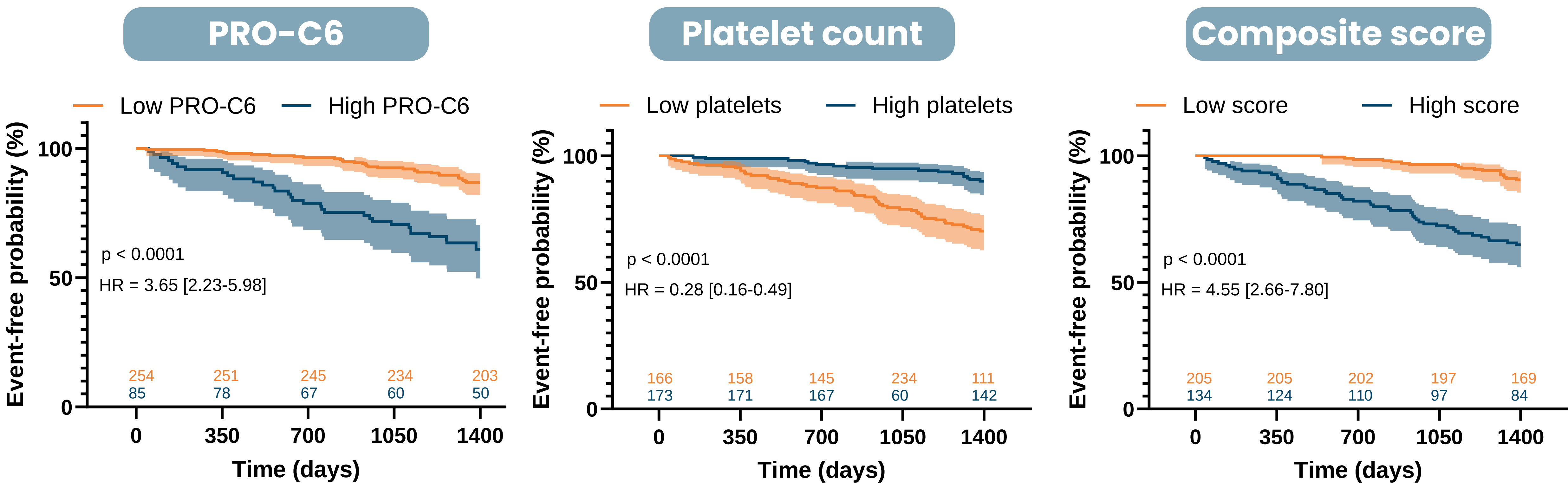


Figure 1: Kaplan-Meier curves, stratifying all patients (n = 339) by high and low PRO-C6 using 15.0 ng/mL as a cut-off. Multivariable cox regression adjusted for age, gender, BMI and alcohol consumption.

Figure 2: Kaplan-Meier curves, stratifying all patients (n = 339) by high and low platelet count using 155 x 10³ /μL as a cut-off. Multivariable cox regression adjusted for age, gender, BMI and alcohol consumption.

Figure 2: Kaplan-Meier curves, stratifying all patients (n = 339) by high and low score using 15.0 / 155 = 0.0968 as a cut-off. Multivariable cox regression adjusted for age, gender, BMI and alcohol consumption.

Subgroup of patients with cirrhosis

Cirrhosis subgroup demographics

Table 2.	All patients with cirrhosis, N = 151 ¹	No liver-related event, N = 104 ¹	Liver-related event, N = 47 ¹	p-value ²
Baseline characteristics				
Gender, female	47 (31%)	30 (29%)	17 (36%)	0.4
Age, years	50 (47, 55)	51 (47, 55)	50 (47, 54)	0.4
BMI, kg/m ²	29.3 (26.7, 32.6)	29.0 (25.9, 31.5)	30.6 (27.8, 33.8)	0.021
Alcohol consumption, drinks/week	4.6 (0.8, 14.2)	4.5 (0.7, 12.8)	5 (1.1, 24.1)	0.4
ALT, U/L	90 (65, 133)	99 (64, 134)	83 (68, 125)	0.5
ALT, U/L	82 (60, 114)	77 (58, 100)	92 (66, 120)	0.061
Platelet count, x10 ³ /μL	133 (92, 176)	141 (114, 179)	95 (81, 147)	<0.001
PRO-C6, ng/mL	13.3 (10.7, 17.2)	12.2 (10.5, 15.0)	16.6 (11.6, 18.8)	<0.001

¹ n (%); Median (IQR), ²Pearson's Chi-squared test; Mann-Whitney U test.

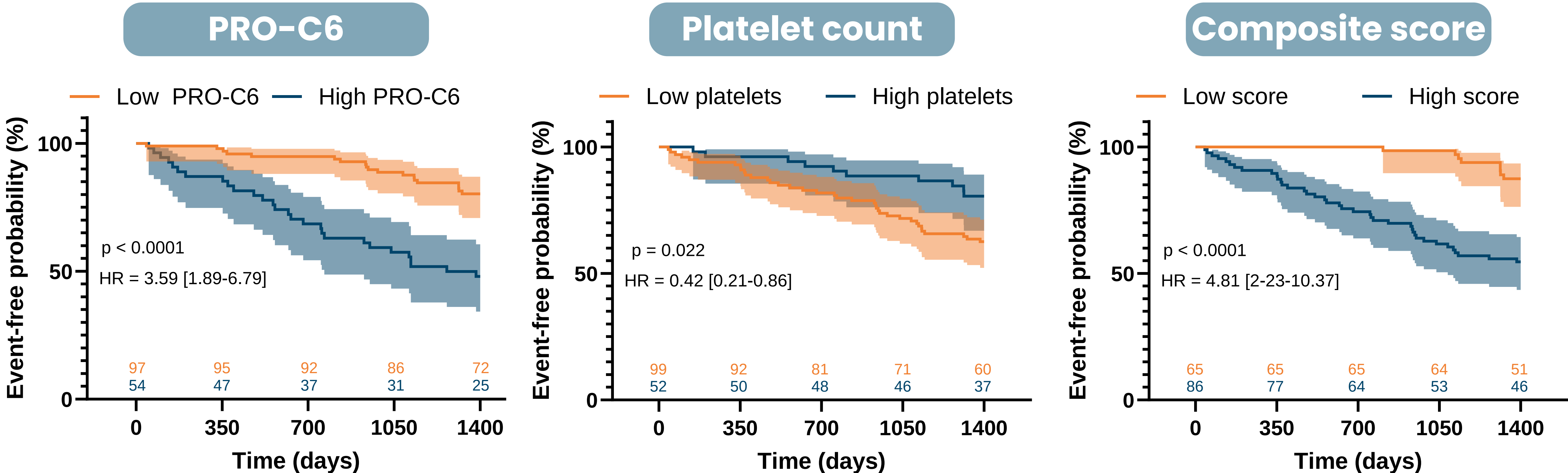


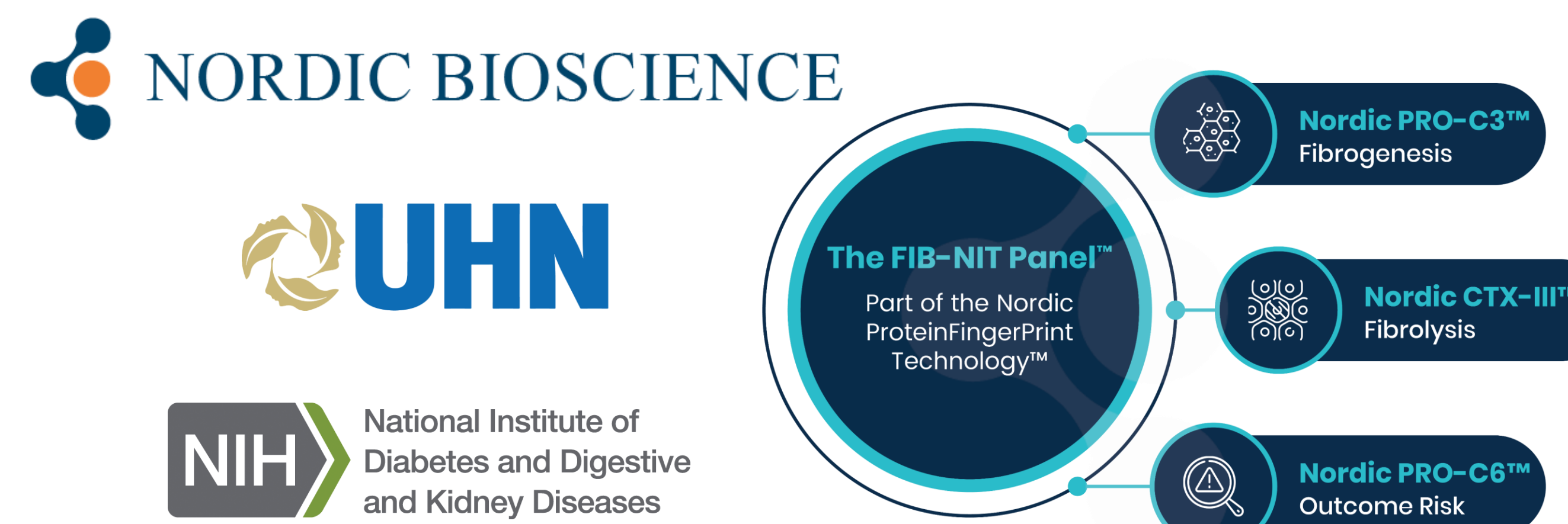
Figure 4: Kaplan-Meier curves, stratifying patients with cirrhosis (n = 151) by high and low PRO-C6 using 15.0 ng/mL as a cut-off. Multivariable cox regression adjusted for age, gender, BMI and alcohol consumption.

Figure 5: Kaplan-Meier curves, stratifying patients with cirrhosis (n = 151) by high and low platelet count using 155 x 10³ /μL as a cut-off. Multivariable cox regression adjusted for age, gender, BMI and alcohol consumption.

Figure 6: Kaplan-Meier curves, stratifying patients with cirrhosis (n = 151) by high and low score using 15.0 / 155 = 0.0968 as a cut-off. Multivariable cox regression adjusted for age, gender, BMI and alcohol consumption.

KEY MESSAGES

- A composite score combining PRO-C6 and platelet count improved prognosis of liver-related outcomes in patients with chronic hepatitis C (CHC) cirrhosis compared to PRO-C6 or platelet count alone
- In CHC patients with cirrhosis, no liver-related outcomes were observed in the low-score group for more than two years.
- PRO-C6/platelet count may help better risk stratify CHC patients with advanced disease for liver-related outcomes.
- Validation of the prognostic utility of our PRO-C6/platelet count composite score in CHC patients after sustained virologic response and other advanced stage chronic liver disease is required.



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