Appendix A

Subgroup Analyses-Multivariate Cox Regression

NSBB *vs* SBB

Table 1 Multivariate Cox regression predicting the first hepatic encephalopathy-related readmission in patients on NSBB *vs* SBB (*n* = 161)

Variable	**Adjusted**	
	HR (95%CI)	***P* value**
Age, years		
Gender, male		
MELD-Na score (reference: MELD-Na score < 15)		
15 ≤ MELD-Na score ≤ 24		
25 ≤ MELD-Na score ≤ 34		
MELD-Na score > 34		
History of TIPS, presence of	1.74 (0.99-3.07)	0.055
NSBB use, presence of (*vs* SBB use)	1.673 (1.004-2.788)	0.048

Abbreviations: HR, Hazard ratio; MELD-Na, Model for End-Stage Liver Disease-Sodium; NSBB, nonselective beta-blocker; SBB, selective beta-blocker; TIPS, transjugular intrahepatic portosystemic shunt.

Ascites

Table 2 Multivariate Cox regression predicting the first hepatic encephalopathy-related readmission in patients with ascites (*n* = 144)

Variable	Adjusted	
	HR (95%CI)	***P* value**
Age, years		
Gender, male		
MELD-Na score (reference: MELD-Na score < 15)		
15 ≤ MELD-Na score ≤ 24		
25 ≤ MELD-Na score ≤ 34		
MELD-Na score > 34		
History of TIPS, presence of		
NSBB use, presence of	1.67 (1.03-2.70)	0.04

Abbreviations: HR, Hazard ratio; MELD-Na, Model for End-Stage Liver Disease-Sodium; NSBB, nonselective beta-blocker; TIPS, transjugular intrahepatic portosystemic shunt.

Table 3 Multivariate Cox regression predicting the first hepatic encephalopathy-related readmission in patients without ascites (*n* = 249)

Variable	Adjusted	
	HR (95%CI)	***P* value**
Age, years		
Gender, male		
MELD-Na score (reference: MELD-Na score < 15)		
15 ≤ MELD-Na score ≤ 24		
25 ≤ MELD-Na score ≤ 34		
MELD-Na score > 34		
History of TIPS, presence of	1.84 (1.14-2.98)	0.013
NSBB use, presence of	1.88 (1.31-2.71)	0.001

Abbreviations: HR, Hazard ratio; MELD-Na, Model for End-Stage Liver Disease-Sodium; NSBB, nonselective beta-blocker; TIPS, transjugular intrahepatic portosystemic shunt.

Esophageal varices

Table 4 Multivariate Cox regression predicting the first hepatic encephalopathy-related readmission in patients with history of esophageal varices (*n* = 154)

Variable	Adjusted	
	HR (95%CI)	***P* value**
Age, years		
Gender, male		
MELD-Na score (reference: MELD-Na score < 15)		
15 ≤ MELD-Na score ≤ 24	1.62 (0.94-2.81)	0.08
25 ≤ MELD-Na score ≤ 34		
MELD-Na score > 34		
History of TIPS, presence of		
NSBB use, presence of	1.71 (1.08-2.72)	0.02

Abbreviations: HR, Hazard ratio; MELD-Na, Model for End-Stage Liver Disease-Sodium; NSBB, nonselective beta-blocker; TIPS, transjugular intrahepatic portosystemic shunt.

Table 5 Multivariate Cox regression predicting the first hepatic encephalopathy-related readmission in patients without history of esophageal varices (*n* = 239)

Variable	Adjusted	
	HR (95%CI)	***P* value**
Age, years		
Gender, male		
MELD-Na score (reference: MELD-Na score < 15)		
15 ≤ MELD-Na score ≤ 24		
25 ≤ MELD-Na score ≤ 34		
MELD-Na score > 34		
History of TIPS, presence of	2.28 (1.26-4.12)	0.007
NSBB use, presence of	2.01 (1.33-3.03)	0.001

Abbreviations: HR, Hazard ratio; MELD-Na, Model for End-Stage Liver Disease-Sodium; NSBB, nonselective beta-blocker; TIPS, transjugular intrahepatic portosystemic shunt.

MELD-Na (Median value: 22)

Table 6 Multivariate Cox regression predicting the first hepatic encephalopathy-related readmission in patients with MELD-Na < 22 (*n* = 184)

Variable	Adjusted	
	HR (95%CI)	***P* value**
Age, years		
Gender, male		
History of TIPS, presence of	1.661 (0.997-2.768)	0.052
NSBB use, presence of	1.62 (1.10-2.40)	0.015

Abbreviations: HR, Hazard ratio; MELD-Na, Model for End-Stage Liver Disease-Sodium; NSBB, nonselective beta-blocker; TIPS, transjugular intrahepatic portosystemic shunt.

Table 7 Multivariate Cox regression predicting the first hepatic encephalopathy-related readmission in patients with MELD-Na ≥ 22 (*n* = 188)

Variable	Adjusted	
	HR (95%CI)	***P* value**
Age, years		
Gender, male		
History of TIPS, presence of		
NSBB use, presence of	2.21 (1.39-3.52)	0.001

Abbreviations: HR, Hazard ratio; MELD-Na, Model for End-Stage Liver Disease-Sodium; NSBB, nonselective beta-blocker; TIPS, transjugular intrahepatic portosystemic shunt.

Lactulose use

Table 8 Multivariate Cox regression predicting the first hepatic encephalopathy-related readmission in patients with lactulose use (*n* = 285)

Variable	Adjusted	
	HR (95%CI)	***P* value**
Age, years		
Gender, male		
MELD-Na score (reference: MELD-Na score < 15)		
15 ≤ MELD-Na score ≤ 24		
25 ≤ MELD-Na score ≤ 34		
MELD-Na score > 34		
History of TIPS, presence of		
NSBB use, presence of	1.73 (1.25-2.40)	0.001

Abbreviations: HR, Hazard ratio; MELD-Na, Model for End-Stage Liver Disease-Sodium; NSBB, nonselective beta-blocker; TIPS, transjugular intrahepatic portosystemic shunt.

Rifaximin use

Table 9 Multivariate Cox regression predicting the first hepatic encephalopathy-related readmission in patients with rifaximin use (*n* = 208)

Variable	Adjusted	
	HR (95%CI)	***P* value**
Age, years		
Gender, male		
MELD-Na score (reference: MELD-Na score < 15)		
15 ≤ MELD-Na score ≤ 24		
25 ≤ MELD-Na score ≤ 34		
MELD-Na score > 34		
History of TIPS, presence of		
NSBB use, presence of	2.06 (1.39-3.05)	< 0.001

Abbreviations: HR, Hazard ratio; MELD-Na, Model for End-Stage Liver Disease-Sodium; NSBB, nonselective beta-blocker; TIPS, transjugular intrahepatic portosystemic shunt.

Appendix B

Subgroup Analyses-Negative Binomial Generalized Regression

NSBB *vs* SBB

Table 10 Negative binomial generalized regression model predicting hepatic encephalopathy-related admissions per person-month in patients on NSBB *vs* SBB (*n* = 179)

Variable	IRR (95%CI)	*P* value	*B*
Age, years	0.977 (0.956-1.000)	0.046	- 0.023
Gender, male	1.30 (0.86-1.95)	0.21	0.260
MELD-Na score	1.05 (1.02-1.08)	0.003	0.044
History of TIPS, presence of	1.65 (0.90-3.03)	0.11	0.499
NSBB use, presence of (*vs* SBB use)	1.85 (1.14-3.01)	0.01	0.614

Abbreviations: IRR, incidence rate ratio; MELD-Na, Model for End-Stage Liver Disease-Sodium; NSBB, nonselective beta-blocker; SBB, selective beta-blocker; TIPS, transjugular intrahepatic portosystemic shunt.

Ascites

Table 11 Negative binomial generalized regression model predicting hepatic encephalopathy-related admissions per person-month in patients with ascites (*n* = 144)

Variable	IRR (95%CI)	*P* value	B
Age, years	0.99 (0.96-1.01)	0.21	- 0.015
Gender, male	0.96 (0.57-1.63)	0.89	- 0.036
MELD-Na score	1.07 (1.04-1.12)	< 0.001	0.072
History of TIPS, presence of	1.47 (0.65-3.37)	0.36	0.387
NSBB use, presence of	1.70 (1.01-2.86)	0.047	0.530

Abbreviations: IRR, incidence rate ratio; MELD-Na, Model for End-Stage Liver Disease-Sodium; NSBB, nonselective beta-blocker; TIPS, transjugular intrahepatic portosystemic shunt.

Table 12 Negative binomial generalized regression model predicting hepatic encephalopathy-related admissions per person-month in patients without ascites (*n* = 243)

Variable	IRR (95%CI)	*P* value	B
Age, years	0.99 (0.97-1.01)	0.38	- 0.009
Gender, male	1.32 (0.91-1.90)	0.14	0.274
MELD-Na score	1.04 (1.01-1.07)	0.005	0.037
History of TIPS, presence of	2.16 (1.29-3.64)	0.004	0.771
NSBB use, presence of	1.65 (1.51-2.36)	0.006	0.499

Abbreviations: IRR, incidence rate ratio; MELD-Na, Model for End-Stage Liver Disease-Sodium; NSBB, nonselective beta-blocker; TIPS, transjugular intrahepatic portosystemic shunt.

Esophageal varices

Table 13 Negative binomial generalized regression model predicting hepatic encephalopathy-related admissions per person-month in patients with history of esophageal varices (*n* = 152)

Variable	IRR (95%CI)	*P* value	B
Age, years	0.98 (0.96-1.00)	0.83	- 0.021
Gender, male	1.55 (0.98-2.46)	0.060	0.440
MELD-Na score	1.06 (1.03-1.10)	< 0.001	0.061
History of TIPS, presence of	1.45 (0.80-2.62)	0.22	0.370
NSBB use, presence of	1.89 (1.21-2.94)	0.005	0.634

Abbreviations: IRR, incidence rate ratio; MELD-Na, Model for End-Stage Liver Disease-Sodium; NSBB, nonselective beta-blocker; TIPS, transjugular intrahepatic portosystemic shunt.

Table 14 Negative binomial generalized regression model predicting hepatic encephalopathy-related admissions per person-month in patients without history of esophageal varices (*n* = 235)

Variable	IRR (95%CI)	*P* value	B
Age, years	0.99 (0.97-1.01)	0.52	- 0.006
Gender, male	0.88 (0.60-1.30)	0.53	- 0.125
MELD-Na score	1.05 (1.03-1.08)	< 0.001	0.051
History of TIPS, presence of	2.95 (1.53-5.67)	0.001	1.081
NSBB use, presence of	1.52 (1.01-2.30)	0.043	0.424

Abbreviations: IRR, incidence rate ratio; MELD-Na, Model for End-Stage Liver Disease-Sodium; NSBB, nonselective beta-blocker; TIPS, transjugular intrahepatic portosystemic shunt.

MELD-Na (Median value: 22)

Table 15 Negative binomial generalized regression model predicting hepatic encephalopathy-related admissions per person-month in patients with MELD-Na score ≤ 22 (*n* = 204)

Variable	IRR (95%CI)	*P* value	B
Age, years	0.98 (0.96-0.99)	0.007	- 0.025
Gender, male	0.86 (0.59-1.26)	0.44	- 0.151
MELD-Na score	1.07 (1.03-1.12)	0.001	0.071
History of TIPS, presence of	2.12 (1.25-3.60)	0.006	0.750
NSBB use, presence of	1.45 (1.01-2.09)	0.045	0.373

Abbreviations: IRR, incidence rate ratio; MELD-Na, Model for End-Stage Liver Disease-Sodium; NSBB, nonselective beta-blocker; TIPS, transjugular intrahepatic portosystemic shunt.

Table 16 Negative binomial generalized regression model predicting hepatic encephalopathy-related admissions per person-month in patients with MELD-Na score > 22 (*n* = 168)

Variable	IRR (95%CI)	*P* value	B
Age, years	1.01 (0.98-1.03)	0.69	0.006
Gender, male	1.77 (1.05-2.97)	0.03	0.570
MELD-Na score	1.08 (1.02-1.13)	0.005	0.074
History of TIPS, presence of	1.48 (0.62-3.50)	0.38	0.390
NSBB use, presence of	1.77 (1.03-3.02)	0.04	0.568

Abbreviations: IRR, incidence rate ratio; MELD-Na, Model for End-Stage Liver Disease-Sodium; NSBB, nonselective beta-blocker; TIPS, transjugular intrahepatic portosystemic shunt.

Lactulose use

Table 17 Negative binomial generalized regression model predicting hepatic encephalopathy-related admissions per person-month in patients with lactulose use (*n* = 280)

Variable	IRR (95%CI)	*P* value	B
Age, years	0.99 (0.97-1.01)	0.29	- 0.010
Gender, male	1.31 (0.94-1.84)	0.12	0.272
MELD-Na score	1.05 (1.02-1.07)	< 0.001	0.044
History of TIPS, presence of	1.94 (1.22-3.08)	0.005	0.662
NSBB use, presence of	1.80 (1.29-2.51)	0.001	0.588

Abbreviations: IRR, incidence rate ratio; MELD-Na, Model for End-Stage Liver Disease-Sodium; NSBB, nonselective beta-blocker; TIPS, transjugular intrahepatic portosystemic shunt.

Rifaximin use

Table 18 Negative binomial generalized regression model predicting hepatic encephalopathy-related admissions per person-month in patients with rifaximin use (*n* = 207)

Variable	IRR (95%CI)	*P* value	B
Age, years	0.977 (0.958-0.997)	0.02	- 0.023
Gender, male	1.30 (0.88-1.92)	0.19	0.263
MELD-Na score	1.04 (1.01-1.07)	0.01	0.035
History of TIPS, presence of	1.96 (1.16-3.32)	0.01	0.673
NSBB use, presence of	1.73 (1.17-2.53)	0.005	0.545

Abbreviations: IRR, incidence rate ratio; MELD-Na, Model for End-Stage Liver Disease-Sodium; NSBB, nonselective beta-blocker; TIPS, transjugular intrahepatic portosystemic shunt.