

Linear Regression Analysis

RPR Baseline (Mean ± SD)	RPR on first DE (Mean ± SD)	P-value*	DELTA % RPR (Mean ± SD)
0.780	0.886	<0.001	+69.81
0.284	0.283		28.28

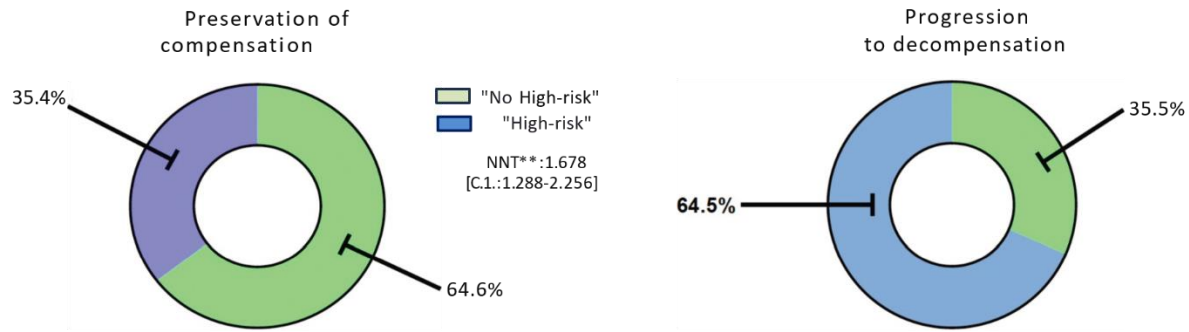
LSM Baseline (Mean ± SD) (kPa)	LSM on first DE (Mean ± SD) (kPa)	P-value*	DELTA % LSM (Mean ± SD)
23.10	24.16	<0.001	+28.88
4.41	4.396		6.61

SD: Standard Deviation; RPR: Red cell distribution width /Platelet ratio; LSM: Liver Stiffness Measurement; kPa: kilopascal; DE: decompensation event*
Wilcoxon test

Supplementary Figure 1 Relationship between RPR and LSM-assessed liver disease progression. RPR: Red cell distribution width to platelet ratio; LSM: Liver Stiffness Measurement.

A

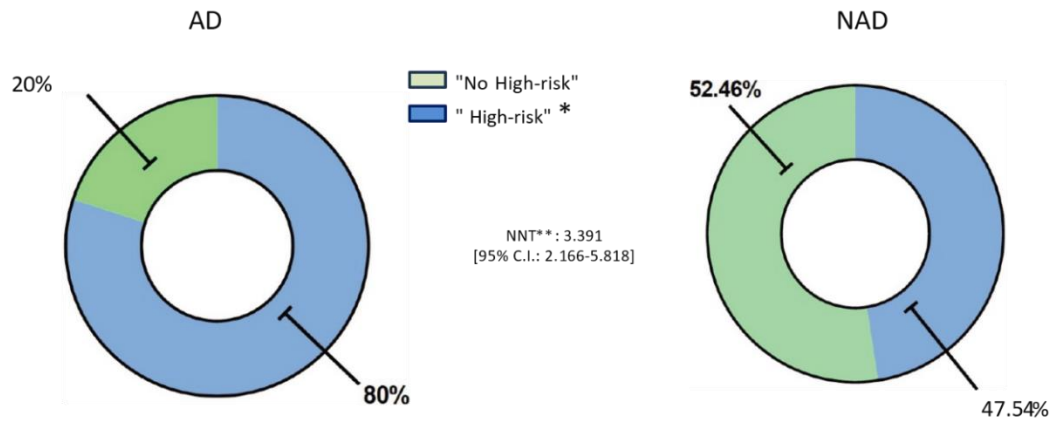
Chi-square test: $p=0.0001$



*Clinically significant portai hyertension (CSPH) defined by the presence of varices evidenced by EGDS
** Reciprocai of attributable risk (*Newcombe/Wi/son with CC analysis*)

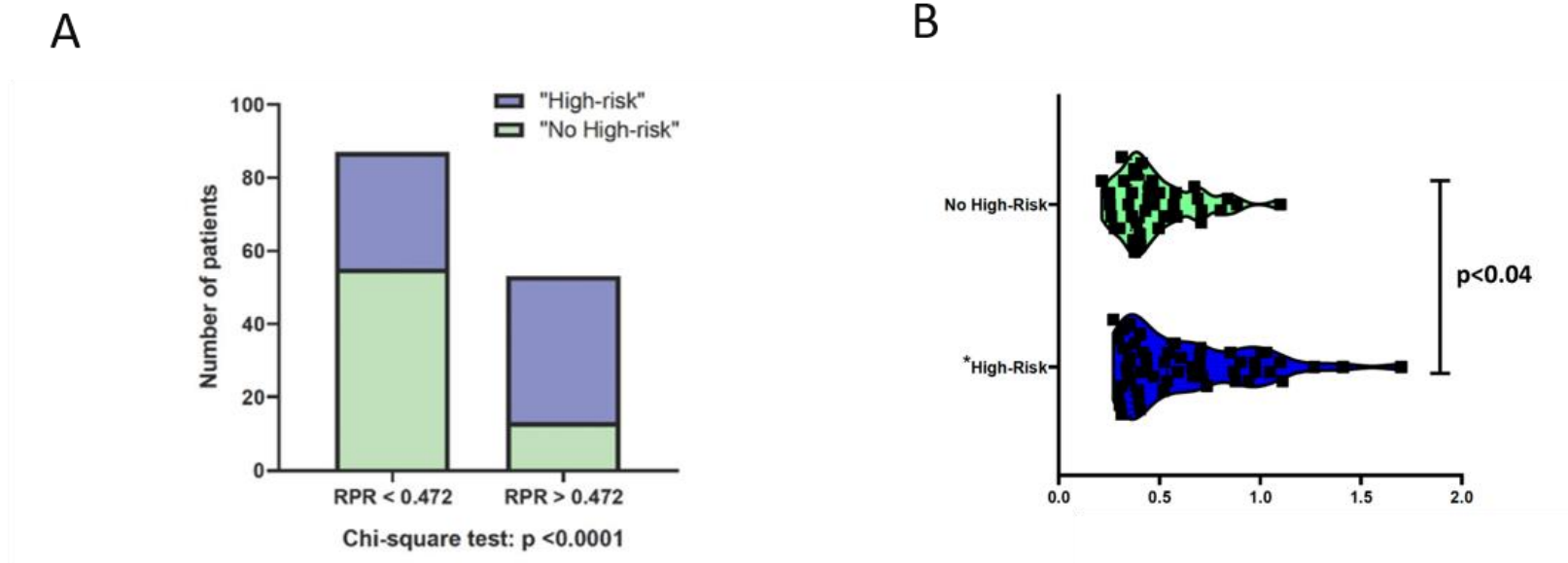
B

Chi-square test: $p= 0035$



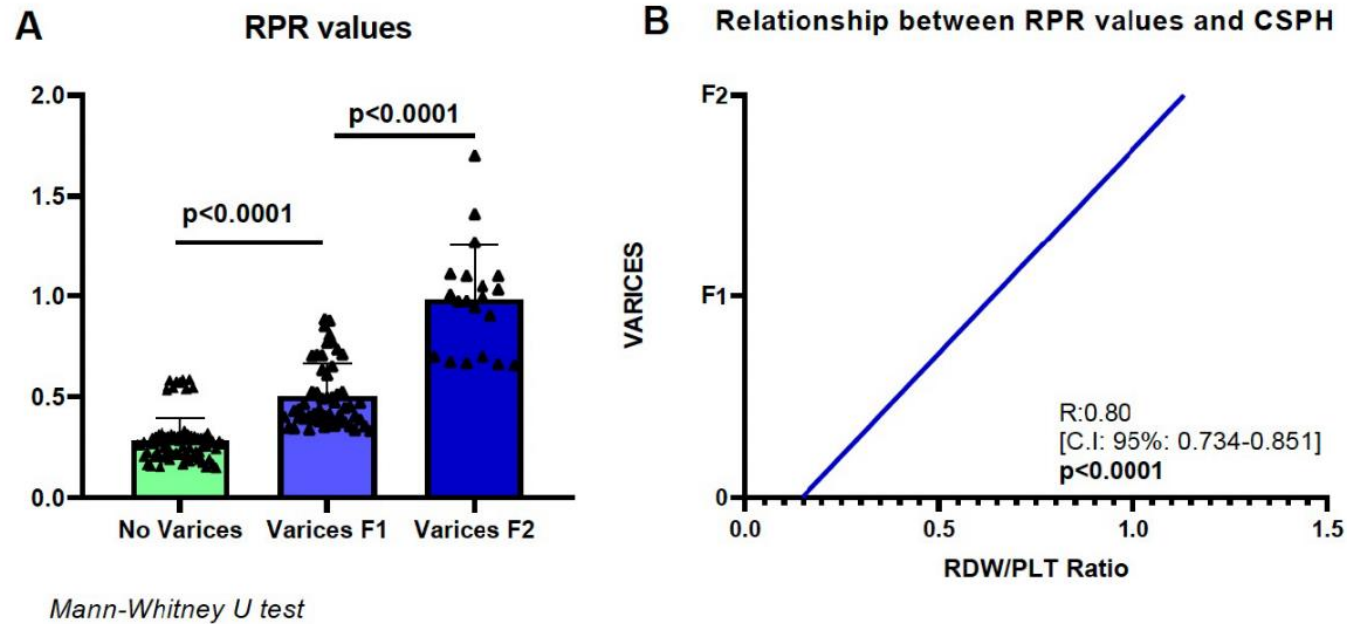
*Clinically significant portai hyertension (CSPH) defined by the presence of varices evidenced by EGDS
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Supplementary Figure 2 Prevalence of patients progressing to dACLD in comparison to individuals remaining compensated. Baseline CSPH in patients remaining cACLD vs patients progressing to decompensation (A). Baseline CSPH in patients progressing AD-decompensating vs patients NAD-decompensating (B). dACLD: decompensated advanced chronic liver disease; CSPH: clinically significant portal hypertension; AD: Acute decompensation; NAD: Non-acute decompensation.



*Clinically significant portai hyertension (CSPH) defined by the presence of varices evidenced by EGDS

Supplementary Figure 3 RPR values in patients presenting baseline CSPH compared to individuals without esophageal varices. Prevalence of baseline CSPH according to baseline RPR values (A); RDW/PLT ratio baseline values, stratified according to the baseline presence/absence of CSPH in patients progressing to dACLD during the 3-year (B). RPR: Red cell distribution width to platelet ratio; CSPH: clinically significant portal hypertension; dACLD: decompensated advanced chronic liver disease.



CSPH: Clinically Significant Portal Hypertension (CSPH) defined by EGDS-evidenced esophageal varices
 RPR: RDW/PLT ratio

Supplementary Figure 4 Relationship between RPR values and CSPH in esophageal varices severity. RPR baseline values across the increased esophageal varices severity (no varices = 0; 1: F1; 2: F2) (A); Correlation between RPR and esophageal varices severity (B). RPR: Red cell distribution width to platelet ratio; CSPH: clinically significant portal hypertension.

Supplementary Table 1 The “ongoing” therapies/medications received by each patient before the enrolment

ID	Medications	ID	Medications	ID	Medications	ID	Medications	ID	Medications
1	Insulin; (1); (3)	36	Diuretics; CCB	71	Insulin; (1)	106	Statin; Ezetimibe	141	Insulin; (3)
2	Metformin; (2)	37	Diuretics; (2);	72	Insulin; (4); (3)	107	Diuretics; ACE-i;	142	Metformin; (4)
3	Metformin; Ezetimibe	38	Insulin; (3); (8)	73	Insulin; (3)	108	Diuretics; (4); (0)	143	Metformin; Ezetimibe
4	Statin; Ezetimibe	39	Metformin; (1); (3)	74	Metformin + Vildagliptin	109	Diuretics; (6A); (9)	144	Diuretics; (9); (2)
5	Diuretics; ACE-i;	40	Metformin; (0)	75	Insulin; (4); (3)	110	(10)	145	Ezetimibe ;(1)
6	CCB; (1); (3); (5)	41	(8) + (10)	76	Insulin; (1); (3)	111	Statin; (9)	146	Metformin + Sitagliptin;(0)
7	Diuretics; ACE-i;	42	Diuretics; CCB	77	Insulin; (2)	112	(10)	147	Insulin; (0)
8	ACE-i; (1); (2); (4)	43	ACE-i; (0)	78	Metformin; (9)	113	Diuretics; (3);	148	Insulin; (1); (3)
9	Diuretics; CCB; (0)	44	Statin; Ezetimibe	79	Metformin; statin	114	Insulin; (1); (3)	149	Insulin; (3); (0)
10	Diuretics; (1); (3)	45	Insulin; Ezetimibe	80	Metformin; (2)	115	Metformin; (5)	150	Statin; Ezetimibe; (5)
11	Insulin; (1); (3)	46	Metformin; (0)	81	Insulin; Diuretics; ACE-i	116	Metformin + glimepiride		
12	Metformin + Sitagliptin; (2); (5)	47	Metformin; (1); (3)	82	Insulin; (5)	117	Insulin; Ezetimibe; (3)		

13	Insulin	48	Diuretics; ACE-i;(0)	83	Insulin; statin; (1); (3)	118	(10)
14	ACE-i; (1); (3)	49	Insulin; (1); (3); (5)	84	Metformin; (2); (0)	119	Statin; Ezetimibe; (2)
15	Diuretics; (2); (0)	50	Metformin; Ezetimibe	85	Metformin + Glimepiride	120	Diuretics; (6A); (6B)
16	Diuretics; CCB	51	Metformin; (9)	86	Insulin; (0)	121	Statin; (1); (3)
17	Insulin; Diuretics; ACE-i	52	Insulin; Diuretics; ACE-i	87	Insulin; (3); (0)	122	(1); (3); (6A)
18	Diuretics; (7A); (7B)	53	Diuretics; (0)	88	Insulin; (5)	123	Diuretics; (5)
19	Insulin; (1); (4)	54	Diuretics; (8)	89	Metformin + Sitagliptin	124	CCB; Diuretics
20	Metformin + Sitagliptin	55	Insulin; statin; (5); (0)	90	Insulin; (2); (0)	125	Insulin
21	Insulin; (8)	56	Insulin; (1); (3)	91	Insulin; Ezetimibe; (9)	126	Insulin; (9)
22	Statin; Ezetimibe	57	Insulin; (3); (1)	92	(4); (5)	127	Insulin; (8); (2)
23	Statin; (1); (3)	58	Insulin; (1); (3)	93	Diuretics; (3)	128	Metformin; (9)
24	Statin; Fibrate	59	Insulin; (1); (3)	94	Insulin; statin; (9)	129	Insulin; (5)

25	Insulin; (4); (8)	60	Insulin; (8)	95	Metformin + Sitagliptin	130	Insulin; (9); (0)
26	Insulin; (2)	61	Metformin; Ezetimibe	96	Insulin; (9); (4)	131	Diuretics; (3)
27	Insulin; Ezetimibe	62	Statin; Ezetimibe	97	CCB; (3); (0)	132	CCB; (3); (1)
28	Metformin + Vildagliptin	63	Insulin	98	Diuretics; CCB	133	Statin; Ezetimibe
29	Insulin; (2)	64	Metformin + Vildagliptin	99	Statin; Ezetimibe	134	Diuretics; CCB
30	Insulin; (4); (0)	65	Insulin; (1); (3)	100	Metformin + Glimepiride	135	Insulin; (6A);
31	Insulin; Ezetimibe	66	Diuretics; (4)	101	Diuretics; (0)	136	Insulin; (0)
32	Metformin + Sitagliptin	67	Diuretics; (8)	102	Insulin; statin; Fibrate	137	Insulin; Ezetimibe
33	Insulin; (1); (3)	68	CCB; (6A)	103	CCB; (9); (3)	138	Metformin; statin
34	Metformin; (8)	69	Statin; Ezetimibe; Fibrate	104	CCB; (1); (3)	139	Insulin; (6B)
35	Insulin; (3)	70	Diuretics; CCB	105	Diuretics;	140	Insulin; statin; (0)

Abbreviations: CCB (calcium channel blockers); ACE-i: Angiotensin Converting Enzyme inhibitors

* **“Others” medications synthetically and schematically included:**

- (0) Nonselective beta-blockers (including propranolol and carvedilol)
- (1) Acetylsalicylic acid (ASA)
- (2) Antibiotics (excluding Rifaximin)
- (3) Proton Pump Inhibitors (PPI)
- (4) Vitamins (D and B)
- (5) Non-steroidal anti-inflammatory drugs (NSAIDs)
- (6A) Systemic steroids
- (6B) Local/Topic steroids
- (7A) Selective Serotonin Reuptake Inhibitors
- (7B) Benzodiazepine (BDZ)
- (8) Antihistamines
- (9) Laxatives (Excluding lactulose)
- (10) Not specifically declared or reported by the relative ID patie

Main “Dysmetabolic” comorbidities prevalence in MASLD enrolled patients:

- Diabetes Mellitus Type 2 = 54.6% (n=82)
- Primary hypertension = 50.6% (n=76),
- Dyslipidemia = 32 % (n=48)

Supplementary Table 2 Predictors of decompensation in MASLD-related compensated advanced chronic liver disease (cACLD) patients

Variable	Univariate		Multivariate**		
	Odds Ratio (95% C.I.)	p-value	Adjusted Odds Ratio (95% C.I.)	p-value	
Age	1.04 (0.95-1.07)	0.52	1.06 (0.97-1.11)	0.54	
Sex (Male)	0.78 (0.42-1.12)	0.34	0.83 (0.78-1.22)	0.47	
AST (U/l)	1.02 (0.95-1.04)	0.41	N.A.	/	
ALT (U/l)	1.01 (1.00-1.05)	0.07	N.A.	/	
RDW-SD	1.32 (0.98-1.41)	0.02	1.14 (0.99-1.23)	0.34	
Creatinine	1.17 (0.92-1.24)	0.51	N.A.	/	
Albumin	0.71 (0.45-0.80)	< 0.0001	0.83 (0.67-0.92)	0.52	
Bilirubin	1.32 (1.09-1.47)	0.03	1.26 (1.09-1.32)	0.61	
Platelets	0.88 (0.78-0.93)	0.03	0.93 (0.77-0.98)	0.72	
INR	1.43 (1.21-1.57)	0.06	N.A.	/	
RPR (RDW/PLT ratio)	5.14 (4.98-5.32)	< 0.0001	1.91 (1.72-1.98)	0.002	
ALBI score	3.45 (3.02-3.67)	< 0.0001	1.78 (1.40-1.92)	0.12	
ALBI-FIB-4	2.90 (2.74-3.09)	< 0.0001	1.66 (1.41-1.96)	0.19	
MELD score	1.51 (1.12-1.70)	0.02	1.33 (0.84-1.42)	0.21	
Child-Pugh score	1.88 (1.53-1.97)	0.03	1.59 (1.24-1.88)	0.32	
FIB-4 score	1.56 (1.43-1.65)	0.65	N.A.	/	
LSM	1.87 (1.58-2.02)	0.04	1.71 (1.58-1.84)	0.45	
CSPH (varices*)	4.31 (3.98-4.76)	< 0.0001	1.84 (1.72- 1.91)	0.04	

AST: aspartate aminotransferase, ALT: alanine aminotransferase, PLT: platelets count; CV: Coefficient Variation; RDW: Red-cell distribution width; INR: International Normalized Ratio, LSM: Liver stiffness measurement; APRI: Aspartate aminotransferase/platelet count ratio

index; MELD: Model for End-stage Liver Disease FIB-4: Fibrosis-4; SD: Standard deviation; CSPH: Clinically Significant Portal Hypertension; N.A: Not-applied/Not-assessable (not included in the model); Statistically significant results ($p < 0.05$) are reported in bold; *Defined by the evidence of esophageal varices; **Logistic regression analysis [Confounding variables (sex, age, BMI, diabetes, alcohol intake, the baseline-administration of Non-selective Beta-Blockers)]

Supplementary Table 3 Predictors of AD decompensation in MASLD-related compensated advanced chronic liver disease (cACLD) patients

Variable	Multivariate**	
	Adjusted Odds Ratio (95% C.I.)	p-value
Age	1.09 (0.94-1.16)	0.67
Sex (Male)	0.74 (0.69-1.31)	0.37
RDW-SD	1.31 (0.89-1.38)	0.24
Creatinine	1.46 (1.17-1.53)	0.33
Albumin	0.78 (0.77-0.89)	0.42
Bilirubin	1.17 (1.07-1.35)	0.71
Platelets	0.89 (0.67-0.93)	0.43
INR	0.88 (0.76-1.12)	0.51
RPR (RDW/PLT ratio)	2.11 (1.72-2.22)	0.03
ALBI score	1.58 (1.30-1.74)	0.32
ALBI-FIB-4	1.69 (1.41-1.87)	0.29
MELD score	1.53 (0.94-1.42)	0.41
Child-Pugh score	1.48 (1.32-1.59)	0.52
FIB-4 score	1.44 (1.32- 1.71)	0.28
LSM	1.59 (1.57-1.93)	0.35
CSPH (varices*)	2.04 (1.92- 2.11)	0.003
Entity of varices	1.98 (1.79- 2.06)	0.007

PLT: platelets count; CV: Coefficient Variation; RDW: Red-cell distribution width; INR: International Normalized Ratio, LSM: Liver stiffness measurement; APRI: AST to Platelet Ratio Index; MELD: Model for End-stage Liver Disease FIB-4: Fibrosis-4; SD: Standard deviation; CSPH: Clinically Significant Portal Hypertension; N.A: Not-applied/Not-assessable (not included in the model); Statistically significant results ($p < 0.05$) are reported in bold; *Defined by the evidence of esophageal varices; **Logistic regression analysis [Confounding variables (sex, age, BMI, diabetes, alcohol intake, the baseline-administration of Non-selective Beta-Blockers)]