

Supplementary material

Dynamic changes between Y1 and Y0	Improvers (n = 66)	Stables (n = 87)	Progressors (n = 39)	P-val
Δ body weight (%)	-5 (-13 – -1)	-1 (-4 – 3)	0 (-3 – 5)	< .001 ^{†‡}
Δ WC (%)	-5 (-10 – -1)	0 (-3 – 2)	-3 (-13 – 7)	.002 [†]
Δ AST (%)	-23 (-50 – 4)	-10 (-30 – 7)	12 (-16 – 32)	.001 [‡]
Δ ALT (%)	-34 (-60 – 0)	-16 (-37 – 12)	-8 (-24 – 29)	.002 [‡]
Δ γ GT (%)	-25 (-45 – -2)	-16 (-33 – 10)	-5 (-29 – 22)	.002 [‡]
Δ ALP (%)	0 (-15 – 13)	0 (-12 – 9)	-3 (-13 – 10)	.805
Δ platelets (%)	-4 (-11 – 6)	1 (-5 – 8)	7 (-7 – 14)	.039 [‡]
Δ HOMA-IR (%) (non-diabetic)	-25 (-53 – 24)	-4 (-29 – 22)	19 (-39 – 35)	.696
Δ TG (%)	-15 (-31 – 26)	-3 (-29 – 27)	5 (-31 – 35)	.809
Δ HDL-c (%)	6 (-7 – 17)	0 (-8 – 10)	0 (-3 – 16)	.354
Δ LSM (%)	-32 (-44 – -27)	0 (-11 – 8)	50 (36 – 86)	< .001 ^{†‡§}
Δ Agile 3+ (%)	-30 (-61 – -10)	3 (-15 – 31)	111 (60 – 227)	< .001 ^{†‡§}
Δ CAP (%)	-7 (-20 – 3)	-3 (-12 – 7)	-2 (-8 – 6)	.025 [‡]

Table S1: Dynamic relative changes between baseline and one year in improvers, stables and progressors groups. Δ means relative difference compared to baseline. Continuous variables are presented as median (1st – 3rd IQR) and compare using one-way ANOVA with Tukey's post-hoc test or Kruskal-Wallis with Dunn's post-hoc test as appropriate according to distribution. *P*-value is considered significant < .05 and significant pairwise comparisons are indicated in bold font and as follows: (†) Improvers vs. Stables; (‡) Improvers vs. Progressors; (§) Stables vs. Progressors.

Abbreviations: ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; CAP, controlled attenuation parameter; γ GT, gamma-glutamyl transpeptidase; HDL-c, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment for insulin resistance; LSM, liver stiffness measurement; MASLD, metabolic dysfunction-associated steatotic liver disease; S, steatosis level; TG, triglycerides; WC, waist circumference; Y, year.

Baseline characteristics	Improvers (n = 45)	Stables (n = 56)	Progressors (n = 33)	Global p-value
Sex (♂, %)	23 (51)	34 (61)	18 (55)	.616
Age (years)	55 (43 – 65)	55 (46 – 63)	58 (49 – 66)	.704
BMI (kg/m ²)	31.6 (29.9 – 36.1)	30.0 (27.5 – 33.4)	29.7 (26.9 – 32.6)	.015^{†‡}
WC (cm)	112 (105 – 120)	106 (98 – 117)	107 (96 – 115)	.067
Hypertension (%)	28 (62)	27 (48)	19 (49)	.354
Type 2 diabetes (%)	20 (44)	18 (32)	12 (36)	.442
Lipid-lowering agent (%)	21 (47)	20 (35)	11 (33)	.404
Current smokers (%)	5 (11)	8 (14)	4 (12)	.902
Alcohol consumption (IU/week)	0 (0 – 1.5)	0 (0 – 2.3)	0 (0 – 3.5)	.771
AST (IU/L)	43 (28 – 59)	29 (22 – 36)	27 (22 – 32)	< .001^{†‡}
ALT (IU/L)	61 (34 – 75)	42 (28 – 57)	40 (30 – 63)	.018[†]
Platelets (x10 ⁹ /L)	252 (190 – 300)	241 (198 – 279)	233 (201 – 326)	.970
FIB-4	1.23 (0.71 – 2.04)	1.04 (0.70 – 1.36)	.90 (.65 – 1.36)	.063
γGT (IU/L)	57 (39 – 111)	62 (31 – 91)	56 (33 – 121)	.998
ALP (IU/L)	68 (58 – 92)	71 (56 – 89)	80 (66 – 108)	.184
Total bilirubin (mg/dL)	.5 (.33 – .6)	.5 (.4 – .8)	.5 (.4 – .9)	.440
HOMA-IR (non-diabetic)	4.7 (3.7 – 9.7)	3.3 (2.1 – 4.2)	4.5 (3.0 – 5.9)	.016[†]
TG (mg/dL)	159 (112 – 204)	166 (116 – 213)	129 (89 – 171)	.110
HDL-c	41 (37 – 49)	49 (41 – 60)	43 (39 – 51)	.037[†]
LSM (kPa)	10.4 (6.9 – 13.7)	6.4 (5.3 – 7.9)	5.3 (4.3 – 6.4)	< .001^{†‡}
Agile 3+	.42 (.17 – .75)	.12 (.06 – .33)	.11 (.03 – .3)	< .001^{†‡}
CAP (dB/m)	342 (307 – 354)	326 (298 – 359)	342 (289 – 356)	.930
MASLD management followed				
Lifestyle (%)	29 (64)	48 (86)	26 (79)	.040[†]
Dietician (%)	6 (13)	5 (9)	2 (6)	.545
Bariatric surgery (%)	2 (4)	0 (0)	0 (0)	.134
Clinical study (%)	6 (13)	1 (2)	3 (9)	.043[†]
GLP1-RA (%)	0 (0)	2 (3)	1 (3)	.454

Table S2: Baseline characteristics of patients classified as improvers, stables and progressors groups after three years of follow-up. ♂ means male. Continuous variables are presented as median (IQR) and compare using one-way ANOVA with Tukey's post-hoc test or Kruskal-Wallis with Dunn's post-hoc test as

appropriate according to distribution. Categorical variables are presented as number (%), compared using Chi-Square or Fisher's exact test. *P*-value is considered significant < .05 and significant pairwise comparisons are indicated in bold font and as follows: (†) Improvers vs. Stables; (‡) Improvers vs. Progressors; (§) Stables vs. Progressors.

Abbreviations: ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; CAP, controlled attenuation parameter; γ GT, gamma-glutamyl transpeptidase; F, fibrosis level; FIB-4, fibrosis-4 score; GLP1-RA, glucagon-like peptide 1 receptor agonist; HDL-c; high density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment for insulin resistance; IU, international unit; LSM, liver stiffness measurement; MASLD, metabolic dysfunction-associated steatotic liver disease; S, steatosis level; TG, triglycerides; WC, waist circumference.

Dynamic changes between Y3 and Y0	Improvers (n = 45)	Stables (n = 56)	Progressors (n = 33)	Global <i>p</i> -value
Δ body weight (%)	-6 (-12 – -2)	-1 (-3 – 2)	3 (-1 – 8)	< .001 ^{†‡}
Δ WC (%)	-5 (-8 – -1)	1 (-2 – 5)	1 (-2 – 4)	< .001 ^{†‡}
Δ AST (%)	-32 (-52 – -19)	-3 (-29 – 9)	4 (-21 – 39)	< .001 ^{†‡}
Δ ALT (%)	-36 (-58 – -6)	-20 (-44 – 12)	3 (-37 – 34)	.024 [‡]
Δ γGT (%)	-37 (-62 – -12)	-18 (-39 – 9)	-22 (-45 – 29)	.011 [†]
Δ ALP (%)	-9 (-18 – 11)	-1 (-10 – 12)	6 (-15 – 20)	.788
Δ platelets (%)	2 (-8 – 10)	3 (-7 – 9)	-2 (-11 – 6)	.676
Δ HOMA-IR (%) (non-diabetic)	-26 (-64 – 3)	12 (-29 – 76)	-7 (-18 – 91)	.096
Δ TG (%)	-4 (-31 – 34)	-12 (-30 – 22)	14 (-14 – 44)	.284
Δ HDL-c (%)	9 (-1 – 23)	-2 (-10 – 16)	-2 (-11 – 8)	.015 [†]
Δ LSM (%)	-40 (-48 – -28)	-1 (-6 – 11)	41 (29 – 72)	< .001 ^{†‡§}
Δ Agile 3+ (%)	-39 (-64 – -26)	43 (-0.4 – 94)	150 (77 – 543)	< .001 ^{†‡§}
Δ CAP (%)	-8 (-16 – 5)	-8 (-16 – 3)	-1 (-9 – 9)	.092

Table S3: Dynamic relative changes between baseline and three years in improvers, stables and progressors groups. Δ means relative difference compared to baseline. Continuous variables are presented as median (IQR) and compare using one-way ANOVA with Tukey's post-hoc test or Kruskal-Wallis with Dunn's post-hoc test as appropriate according to distribution. *P*-value is considered significant < .05 and significant pairwise comparisons are indicated in bold font and as follows: (†) Improvers vs. Stables; (‡) Improvers vs. Progressors; (§) Stables vs. Progressors.

Abbreviations: ALP, phosphatase alkaline; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; CAP, controlled attenuation parameter; γGT, gamma-glutamyl transpeptidase; HDL-c, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment for insulin resistance; LSM, liver stiffness measurement; MASLD, metabolic associated-dysfunction steatotic liver disease; S, steatosis level; TG, triglycerides; WC, waist circumference; Y, year.

	Y1 (n = 192)	Y3 (n = 134)	<i>p</i>-value
IMP, n (%)	66 (34.4)	45 (33.6)	.637
STB, n (%)	87 (45.3)	56 (41.8)	
PRO, n (%)	39 (20.3)	33 (24.6)	

Table S4: Proportions of improvers, stables and progressors at one- and three-year follow-up. Categorical variables are presented as number (%), compared using Chi-Square test. *P*-value is considered significant < .05.

Abbreviations: IMP, improvers; PRO, progressors; STB, stables; Y1, one-year follow-up; Y3, three-year follow-up.

Y1	Univariate analysis			Multivariate analysis – Baseline and changes overtime prediction model		
	OR PRO (n = 39) vs. IMP+STB (n = 153)	95% CI	<i>p</i>	OR PRO (n = 39) vs. IMP+STB (n = 153)	95% CI	<i>p</i>
Baseline variables						
Sex (♂)	.783	.382 – 1.58	.497	.758	.300 – 1.870	.549
Age (years)	1.019	.989 – 1.052	.217	1.050	1.010 – 1.10	.012
Body weight (kg)	.989	.969 – 1.008	.254			
BMI (kg/m ²)	.947	.877 – 1.013	.116	1.040	.952 – 1.140	.349
WC (cm)	.984	.955 – 1.011	.253			
Active smoking status	1.315	.869 – 1.963	.191			
Alcohol consumption (IU/week)	1.018	.899 – 1.132	.764			
Past CVE	.463	.071 – 1.726	.277			
T2D	.749	.342 – 1.564	.447			
Lipid-lowering agent	.998	.470 – 2.055	.995			
Hypertension	1.150	.567 – 2.379	.700			
Platelets (x10 ⁹ /L)	1.341	.072 – 26.39	.844			
ALP (IU/L)	1.011	.108 – 9.297	.992			
AST (IU/L)	.565	.094 – 3.085	.516			
ALT (IU/L)	1.320	.324 – 5.381	.699	1.030	1.010 – 1.050	< .001
γGT (IU/L)	1.247	.472 – 3.223	.652			
HOMA-IR	.815	.624 – .987	.034			
TG (mg/dL)	1.001	.998 – 1.004	.528			
HDL-c (mg/dL)	1.001	.972 – 1.028	.943			
Agile 3+	.054	.007 – .295	< .001			
LSM (kPa)	.683	.551 – .816	< .001	.603	.447 – .767	< .001
CAP (dB/m)	.998	.991 – 1.006	.682			
Variables evolution 1Y						
Δ body weight (%)	1.089	1.029 – 1.166	.002	1.110	1.020 – 1.220	.019
Δ AST (%)	1.017	1.008 – 1.027	< .001			
Δ ALT (%)	1.011	1.004 – 1.019	.003	1.010	1.00 – 1.020	.025
Δ γGT (%)	1.006	.999 – 1.014	.069			
Δ CAP (%)	1.021	.999 – 1.045	.069			

Table S5: Univariate and multiple logistic regression models for increased LSM after one-year compared to stables and improved LSM. ♂ means male. Δ means relative difference compared to baseline. All significant parameters from the univariate analysis (except for collinear values) and clinically justified were included in the multiple logistic regression analysis. *P*-value is considered significant < .05 and indicated in bold font.

Abbreviations: ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; CAP, controlled attenuation parameter; CVE, cardiovascular events; γGT, gamma-glutamyl transpeptidase; HDL-c, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment for insulin resistance; IMP, improvers; LSM, liver stiffness measurement; MASLD, metabolic dysfunction-associated steatotic liver disease; PRO, progressors; S, steatosis level; STB, stables; TG, triglycerides; T2D, type 2 diabetes; WC, waist circumference; Y, year.

Y3	Univariate analysis			Multivariate analysis – Baseline and change over time prediction model		
	OR PRO (n = 33) vs. IMP+STB (n = 101)	95% CI	p	OR PRO (n = 33) vs. IMP+STB (n = 101)	95% CI	p
Baseline variables						
Sex (♂)	1.080	.485 – 2.379	.850	.695	.205 – 2.194	.539
Age (years)	1.013	.979 – 1.050	.464	1.021	.971 – 1.077	.418
Body weight (kg)	.988	.964 – 1.010	.280			
BMI (kg/m ²)	.950	.864 – 1.030	.228	1.122	.990 – 1.286	.071
WC (cm)	.983	.949 – 1.017	.338			
Active smoking status	1.433	.917 – 2.231	.113			
Alcohol consumption (IU/week)	1.258	.565 – 2.529	.543			
Past CVE	.818	.177 – 2.831	.766			
T2D	.947	.410 – 2.119	.897			
Lipid-lowering agent	.732	.312 – 1.645	.454			
Hypertension	.787	.356 – 1.733	.551			
Platelets (x10 ⁹ /L)	.761	.027 – 21.15	.871			
ALP (IU/L)	1.012	1.000 – 1.026	.043	1.014	.996 – 1.036	.156
AST (IU/L)	.977	.949 – .999	.044			
ALT (IU/L)	.804	.158 – 3.984	.789	1.021	1.001 – 1.046	.036
γGT (IU/L)	.963	.307 – 2.914	.947			
HOMA-IR	1.011	.861 – 1.160	.880			
TG (mg/dL)	.993	.985 – 1.001	.090			
HDL-c (mg/dL)	.997	.962 – 1.029	.866			
Agile 3+	.108	.014 – .578	.008			
LSM (kPa)	.684	.536 – .833	< .001	.524	.348 – .721	< .001
CAP (dB/m)	.999	.991 – 1.009	.989			
Variables evolution 3Y						
Δ body weight (%)	1.122	1.050 – 1.212	< .001	1.104	1.004 – 1.230	.040
Δ AST (%)	1.016	1.006 – 1.027	.002			
Δ ALT (%)	1.010	1.002 – 1.018	.019	1.011	.999 – 1.023	.070
Δ γGT (%)	1.007	.998 – 1.017	.140			
Δ CAP (%)	1.025	.999 – 1.052	.052			

Table S6: Univariate and multiple logistic regression models for increased LSM after three years compared to stables and improved LSM. ♂ means male. Δ means relative difference compared to baseline. All significant parameters from the univariate analysis (except for collinear values) and clinically justified were included in the multiple logistic regression analysis. P-value is considered significant < .05 and indicated in bold font.

Abbreviations: ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; CAP, controlled attenuation parameter; CVE, cardiovascular events; γGT, gamma-glutamyl transpeptidase; HDL-c, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment for insulin resistance; IMP, improvers; LSM, liver stiffness measurement; MASLD, metabolic dysfunction-associated steatotic liver disease; PRO, progressors; S, steatosis level; STB, stables; TG, triglycerides; T2D, type 2 diabetes; WC, waist circumference; Y, year.