Hepatic decompensation is accelerated in patients with cirrhosis and alpha-1 antitrypsin Pi*MZ genotype

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Fig. S1. Effects of Pi*MS genotype on hepatic decompensation and liver-related death or liver transplant

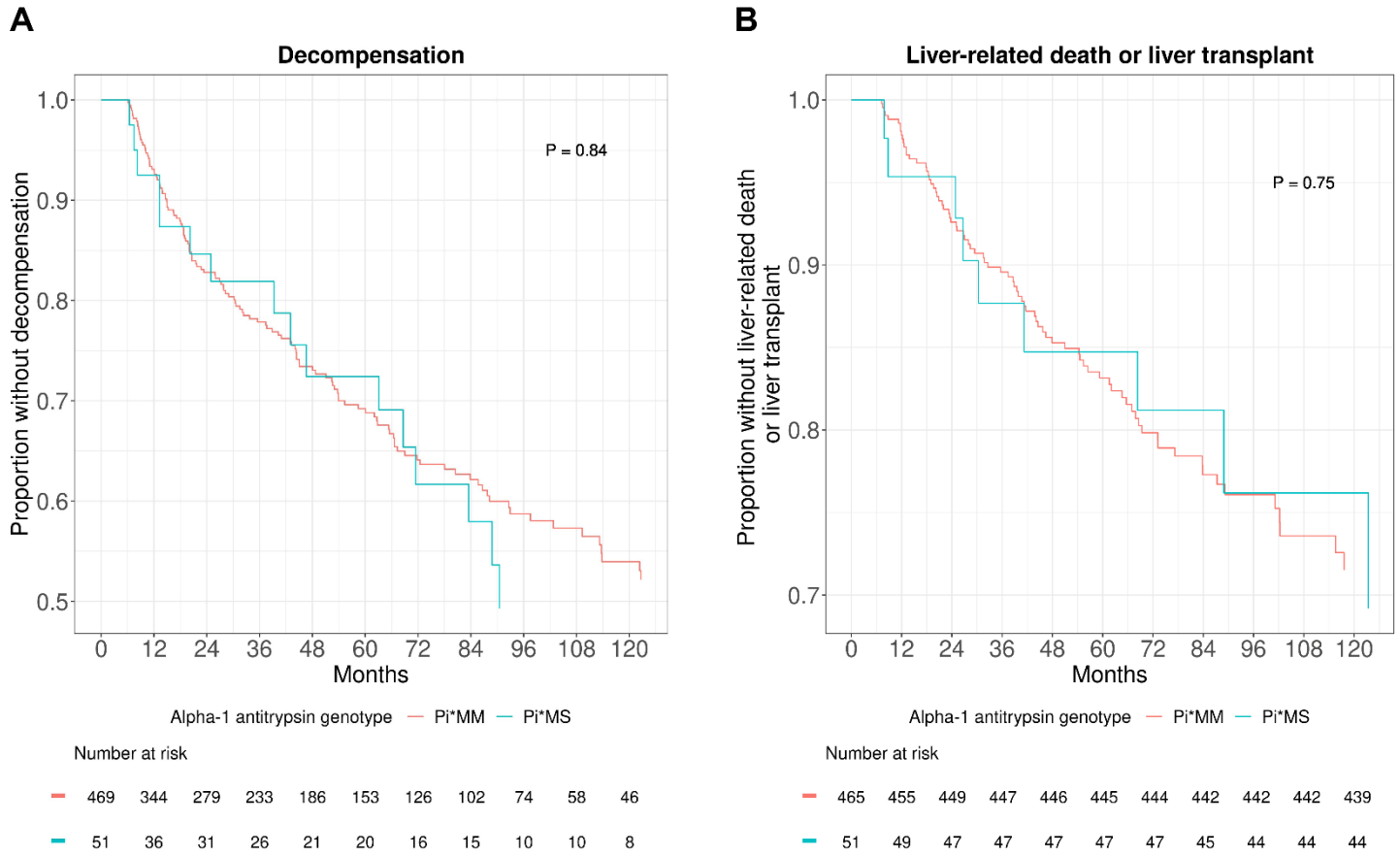

Table S1: Diagnosis codes for cirrhosis, hepatic decompensation, and hepatocellular carcinoma

Disease		ICD-9	ICD-10
Cirrhosis, directly coded		571.2, 571.5, 571.6	K70.30, K70.31, K70.40, K70.41, K71.7, K74.3, K74.4, K74.5, K74.60, K74.69
Portal hypertension	Ascites	789.59	R18.8, K70.31
	Hepatic encephalopathy	572.2	K72.11, K72.90, K72.91
	Varices	456.0, 456.1, 456.20-456.21	I85, I86.4
	Other	572.4, 573.5, 572.3, 567.23	K76.7, K76.81, K76.6, K65.2

ICD, International Classification of Diseases.

Table S2: Effects of Pi*MS genotype on hepatic decompensation and liver-transplant or liver-related death

	Hepatic decompensation		Liver transplant or liver-related death	
Model	Hazard ratio	P value	Hazard ratio	P value
Model 1	1.07 (0.66-1.74)	0.77	1.05 (0.51-2.19)	0.89
Model 2	1.10 (0.66-1.86)	0.71	1.06 (0.50-2.28)	0.88
Model 3	1.32 (0.83-2.09)	0.24	1.22 (0.59-2.53)	0.6
Model 4	1.05 (0.65-1.70)	0.84	0.99 (0.47-2.12)	0.98
Model 5	1.29 (0.82-2.05)	0.27	1.12 (0.52-2.41)	0.77

Hazard ratios (95% confidence interval) for the Pi*MS genotype relative to Pi*MM. Model 1 is adjusted for age, sex, disease etiology (non-alcoholic fatty liver disease or cryptogenic vs. other etiologies), and principal components 1-10. Model 2 is adjusted for model 1 covariates plus albumin. Model 3 is adjusted for model 1 covariates plus platelet count. Model 4 is adjusted for model 1 covariates plus model for end-stage liver disease score. Model 5 is adjusted for model 1 covariates plus platelet count and model for end-stage liver disease score.

Table S3: Effects of Pi*MZ genotype on hepatic decompensation and liver transplant or liver-related death: subgroup analyses

Category		Hepatic decompensation			Liver transplant or liver-related death		
		Hazard ratio	P value	P_{het}	Hazard ratio	P value	P_{het}
Age	< 60 years	1.66 (1.04-2.66)	0.034	0.42	2.12 (0.62-7.29)	0.23	0.64
	>= 60 years	2.31 (1.22-4.38)	0.010		1.43 (0.48-4.30)	0.52	
Sex	Male	2.57 (1.63-4.05)	<0.0001	0.10	2.57 (1.03-6.43)	0.044	0.18
	Female	1.27 (0.63-2.58)	0.51		0.69 (0.13-3.77)	0.67	
Etiology	Non-alcoholic fatty liver disease or cryptogenic	1.88 (0.92-3.83)	0.081	1.00	0.94 (0.13-6.89)	0.95	0.38
	Other	1.88 (1.11-3.16)	0.018		2.51 (1.01-6.27)	0.048	
Diabetes status	Diabetes	1.74 (1.05-2.89)	0.031	0.50	0.99 (0.37-2.67)	0.98	0.042
	No diabetes	1.31 (0.70-2.48)	0.40		7.40 (1.39-39.26)	0.019	
Body mass index	≥ 35 kg/m²	1.91 (1.15-3.16)	0.012	0.87	3.22 (1.05-9.83)	0.04	0.087
	< 35 kg/m²	2.05 (1.05-4.00)	0.035		0.69 (0.18-2.71)	0.59	
Clinically significant portal hypertension	Absent	1.91 (0.98-3.72)	0.056	0.65	1.74 (0.85-3.59)	0.13	0.96
	Present	2.29 (1.53-3.44)	<0.001		1.70 (0.82-3.52)	0.15	

Hazard ratios (95% confidence interval) for the Pi*MZ genotype relative to Pi*MM. Models are adjusted for age, sex (except the sex-specific subgroup analysis), disease etiology (except for the etiology-specific analysis), and principal components 1-10. P_{het} is the p value for heterogeneity between the different age, sex, or etiology categories. Clinically significant portal hypertension was defined as presence of varices or collaterals on endoscopy or imaging, or liver stiffness measurement ≥ 25 kPa on vibration-controlled transient elastography.

Table S4: Effects of Pi*MZ genotype on individual decompensating events

Outcome	Hazard ratio	P value
Ascites	1.82 (1.09-3.05)	0.022
Hepatic encephalopathy	1.54 (0.97-2.43)	0.065
Variceal bleed	1.54 (0.56-4.24)	0.41

Hazard ratios (95% confidence interval) for the Pi*MZ genotype relative to Pi*MM. All models are adjusted for age, sex, disease etiology (non-alcoholic fatty liver disease or cryptogenic vs. other etiologies), and principal components 1-10.