

Supplementary Table 1. Characteristics of HCC patients according to pre-cancer diagnosis statin use

Characteristics	Pre-diagnosis statin non-user (N=12748)	Pre-diagnosis statin user (N=2674)	p-value
Age, Mean (SD)	62.5 (8.4)	69.0 (8.7)	<0.001
BMI, Mean (SD)	26.9 (5.5)	28.9 (5.9)	<0.001
Male, N (%)	12627 (99.1)	2666 (99.7)	0.003
Ethnicity/race			<0.001
White	7381 (57.9)	1662 (62.2)	
Hispanic	1201 (9.4)	257 (9.6)	
Black	3183 (25.0)	565 (21.1)	
Other	264 (2.1)	66 (2.5)	
Missing	719 (5.6)	124 (4.6)	
Alcohol abuse			<0.001
No	7140 (56.0)	1738 (65.0)	
Yes	5608 (44.0)	936 (35.0)	
Smoking status			<0.001
Never	1291 (10.1)	382 (14.3)	
Ever	10953 (85.9)	2269 (84.8)	
Missing	504 (4.0)	23 (0.9)	
NAFLD			0.001
No	11427 (89.6)	2326 (87.0)	
Yes	1321 (10.4)	348 (13.0)	
Hepatitis C infection			<0.001
No	3757 (29.5)	1442 (53.9)	
Yes	8991 (70.5)	1232 (46.1)	
Hepatitis B infection			0.03
No	11555 (90.6)	2460 (92.0)	
Yes	1193 (9.4)	214 (8.0)	
Cirrhosis			<0.001
No	6343 (49.8)	1629 (60.9)	
Yes	6405 (50.2)	1045 (39.1)	
Grade			<0.001
Grade I-II	2996 (23.5)	718 (26.9)	
Grade III-IV	645 (5.1)	164 (6.1)	
Missing	9107 (71.4)	1792 (67.0)	
TNM Stage			<0.001
Stage 1	4160 (32.6)	991 (37.1)	
Stage 2	3269 (25.6)	579 (21.6)	
Stage 3	2134 (16.7)	478 (17.9)	
Stage 4	1305 (10.2)	282 (10.5)	
Missing	1880 (14.8)	344 (12.9)	
Treatment			<0.001
None	3872 (30.4)	722 (27.0)	
Surgery	3262 (25.6)	663 (24.8)	
TACE	2060 (16.2)	459 (17.2)	

	Systemic chemotherapy	551 (4.3)	87 (3.2)	
	Other	3003 (23.6)	743 (27.8)	
MELD score				<0.001
	<10	4111 (32.2)	989 (37.0)	
	≥10	4200 (32.9)	846 (31.6)	
	Missing	4437 (34.8)	839 (31.4)	
APRI				<0.001
	<2	3171 (24.9)	1167 (43.6)	
	≥2	2163 (17.0)	211 (7.9)	
	Missing	7414 (58.2)	1296 (48.5)	
Ascites				<0.001
	No	9537 (74.8)	2190 (81.9)	
	Yes	3211 (25.2)	484 (18.1)	
Varices				<0.001
	No	9556 (75.0)	2241 (83.8)	
	Yes	3192 (25.0)	433 (16.2)	
Encephalopathy				<0.001
	No	11000 (86.3)	2421 (90.5)	
	Yes	1748 (13.7)	253 (9.5)	
Deyo comorbidity index				<0.001
	0-1	5683 (44.6)	710 (26.6)	
	2-3	3078 (24.1)	838 (31.3)	
	4-5	2395 (18.8)	606 (22.7)	
	≥6	1592 (12.5)	520 (19.4)	
ECOG performance status				<0.001
	0	2274 (17.8)	495 (18.5)	
	1	1783 (14.0)	407 (15.2)	
	≥2	587 (4.6)	185 (6.9)	
	Missing	8104 (63.6)	1587 (59.4)	

APRI, AST to Platelet Ratio Index; BMI, body mass index; HCC, Hepatocellular carcinoma; TACE, transarterial chemoembolization; SD, standard deviation. Patients with missing values were excluded from comparisons.

Supplementary Table 2. Unadjusted HRs for associations with cancer specific and all-cause mortality for HCC patients

Characteristics	Cancer specific mortality	All-cause mortality
	Unadjusted HR (95% CI)	Unadjusted HR (95% CI)
Age	1.01 (1.00-1.01)	1.01 (1.01-1.01)
BMI	0.98 (0.97-0.98)	0.99 (0.98-0.99)
Male (vs. Female)	1.79 (1.27-2.52)	1.48 (1.19-1.85)
Ethnicity/race		
White	1.00 (Ref)	1.00 (Ref)
Hispanic	0.86 (0.79-0.94)	0.89 (0.84-0.95)
Black	0.96 (0.90-1.02)	0.95 (0.91-0.99)
Other	0.83 (0.70-1.00)	0.86 (0.76-0.98)
Alcohol abuse		
No	1.00 (Ref)	1.00 (Ref)
Yes	1.09 (1.04-1.15)	1.08 (1.04-1.12)
Smoking status		
Never	1.00 (Ref)	1.00 (Ref)
Ever	1.10 (1.01-1.19)	1.09 (1.03-1.15)
NAFLD		
No	1.00 (Ref)	1.00 (Ref)
Yes	0.95 (0.88-1.03)	0.94 (0.89-1.00)
Hepatitis C infection		
No	1.00 (Ref)	1.00 (Ref)
Yes	0.90 (0.85-0.95)	0.89 (0.86-0.93)
Hepatitis B infection		
No	1.00 (Ref)	1.00 (Ref)
Yes	1.05 (0.97-1.15)	1.01 (0.95-1.07)
Cirrhosis		
No	1.00 (Ref)	1.00 (Ref)
Yes	0.93 (0.88-0.98)	0.97 (0.94-1.01)
Grade		
Grade I-II	1.00 (Ref)	1.00 (Ref)
Grade III-IV	1.48 (1.31-1.66)	1.44 (1.33-1.57)
TNM Stage		
Stage 1	1.00 (Ref)	1.00 (Ref)
Stage 2	1.66 (1.55-1.79)	1.44 (1.37-1.51)
Stage 3	3.38 (3.14-3.64)	2.61 (2.47-2.75)
Stage 4	5.57 (5.13-6.05)	4.04 (3.80-4.30)
Treatment		
None	1.00 (Ref)	1.00 (Ref)
Surgery	0.30 (0.28-0.32)	0.37 (0.35-0.39)
TACE	0.64 (0.59-0.69)	0.63 (0.60-0.67)
Systemic chemotherapy	1.27 (1.13-1.42)	1.13 (1.04-1.23)
Other	0.91 (0.85-0.97)	0.86 (0.82-0.91)
MELD score		

	<10	1.00 (Ref)	1.00 (Ref)
	≥10	1.36 (1.28-1.45)	1.36 (1.30-1.42)
APRI			
	<2	1.00 (Ref)	1.00 (Ref)
	≥2	1.01 (0.94-1.09)	1.07 (1.01-1.13)
Ascites			
	No	1.00 (Ref)	1.00 (Ref)
	Yes	1.84 (1.74-1.94)	1.75 (1.68-1.82)
Varices			
	No	1.00 (Ref)	1.00 (Ref)
	Yes	1.03 (0.97-1.09)	1.10 (1.06-1.15)
Encephalopathy			
	No	1.00 (Ref)	1.00 (Ref)
	Yes	1.57 (1.47-1.69)	1.60 (1.52-1.68)
Deyo comorbidity index			
	0-1	1.00 (Ref)	1.00 (Ref)
	2-3	1.04 (0.98-1.11)	1.03 (0.99-1.08)
	4-5	0.96 (0.90-1.03)	1.04 (0.99-1.09)
	≥6	1.12 (1.03-1.21)	1.22 (1.16-1.29)
ECOG performance status			
	0	1.00 (Ref)	1.00 (Ref)
	1	1.73 (1.57-1.89)	1.41 (1.32-1.51)
	≥2	2.78 (2.46-3.14)	2.30 (2.11-2.51)

APRI, AST to Platelet Ratio Index; BMI, body mass index; CI, confidence interval; HCC, Hepatocellular carcinoma; HR, hazard; TACE, transarterial chemoembolization;

Supplementary Table 3. Stratified analyses of the association between post-diagnosis statin use and mortality in HCC patients

	Cancer-specific mortality	All-cause mortality
	Adjusted HR (95% CI)	Adjusted HR (95% CI)
Pre-diagnosis statin use ¹		
No	0.87 (0.75-1.01)	0.93 (0.84-1.03)
Yes	0.69 (0.60-0.79)	0.74 (0.67-0.82)
TMN Stage ²		
I	0.79 (0.66-0.95)	0.87 (0.78-0.98)
II	0.74 (0.61-0.92)	0.79 (0.69-0.91)
III	0.86 (0.69-1.06)	0.94 (0.80-1.11)
IV	0.75 (0.54-1.03)	0.74 (0.58-0.95)
Treatment ³		
None	0.72 (0.59-0.88)	0.71 (0.61-0.81)
Surgery	0.87 (0.70-1.10)	0.93 (0.81-1.07)
TACE	0.92 (0.74-1.15)	0.92 (0.79-1.09)
Systemic chemotherapy	0.88 (0.51-1.51)	0.78 (0.52-1.19)
Other	0.75 (0.62-0.91)	0.88 (0.78-1.01)
Cirrhosis ⁴		
No	0.79 (0.69-0.90)	0.82 (0.75-0.90)
Yes	0.80 (0.68-0.94)	0.88 (0.79-0.98)
HCV infection ⁵		
No	0.73 (0.63-0.85)	0.75 (0.67-0.83)
Yes	0.85 (0.74-0.98)	0.93 (0.85-1.02)
Alcohol abuse ⁶		
No	0.75 (0.66-0.85)	0.81 (0.74-0.88)
Yes	0.87 (0.74-1.02)	0.91 (0.81-1.01)
NAFLD ⁷		
No	0.80 (0.72-0.89)	0.84 (0.74-0.91)
Yes	0.80 (0.59-1.08)	0.90 (0.73-1.10)
MELD score ⁸		
<10	0.79 (0.67-0.93)	0.86 (0.77-0.96)
≥10	0.75 (0.62-0.89)	0.81 (0.72-0.92)
APRI ⁹		
<2	0.84 (0.71-0.98)	0.85 (0.76-0.95)
≥2	0.80 (0.58-1.09)	1.03 (0.85-1.26)

¹Adjusted for age, gender, race, BMI, alcohol abuse, smoking history, stage, treatment, HBV infection, HCV infection, cirrhosis, NAFLD, and post-diagnosis NSAID and aspirin use (time-varying).

²Adjusted for age, gender, race, BMI, alcohol abuse, smoking history, treatment, HBV infection, HCV infection, cirrhosis, NAFLD, pre-diagnosis statin use, and post-diagnosis NSAID and aspirin use (time-varying).

³Adjusted for age, gender, race, BMI, alcohol abuse, smoking history, stage, HBV infection, HCV infection, cirrhosis, NAFLD, pre-diagnosis statin use, and post-diagnosis NSAID and aspirin use (time-varying).

⁴Adjusted for age, gender, race, BMI, alcohol abuse, smoking history, treatment, HBV infection, HCV infection, stage, NAFLD, pre-diagnosis statin use, and post-diagnosis NSAID and aspirin use (time-varying).

⁵Adjusted for age, gender, race, BMI, alcohol abuse, smoking history, treatment, HBV infection, stage, cirrhosis, NAFLD, pre-diagnosis statin use, and post-diagnosis NSAID and aspirin use (time-varying).

⁶Adjusted for age, gender, race, BMI, smoking history, stage, treatment, HBV infection, HCV infection, cirrhosis, NAFLD, pre-diagnosis statin use, and post-diagnosis NSAID and aspirin use (time-varying).

⁷Adjusted for age, gender, race, BMI, alcohol abuse, smoking history, treatment, HBV infection, HCV infection, cirrhosis, stage, pre-diagnosis statin use, and post-diagnosis NSAID and aspirin use (time-varying).

⁸Adjusted for age, gender, race, BMI, alcohol abuse, smoking history, stage, treatment, HBV infection, HCV infection, cirrhosis, NAFLD, pre-diagnosis statin use, and post-diagnosis NSAID and aspirin use (time-varying).