

Results: At the 2-year landmark, 8.2% of those with baseline MASLD were reclassified to MetALD or ALD, 34.2% of those with baseline MetALD were reclassified to MASLD or ALD, and 64.0% of those with baseline ALD were reclassified to MASLD or MetALD. Among baseline MASLD, the risk of MALO was higher for those reclassified to MetALD (HR 1.55;95% CI 1.40-1.71) or ALD (HR 2.13;95% CI 1.66-2.74) compared with those who remained MASLD. Among baseline MetALD, the risk of MALO was lower for those reclassified to MASLD (HR 0.55;95% CI 0.48-0.64) and higher for those reclassified to ALD (HR 1.80;95% CI 1.58-2.06) compared with those who remained MetALD. Among baseline ALD, the risk of MALO was lower for those reclassified to MASLD (HR 0.31;95% CI 0.21-0.46) or MetALD (HR 0.82;95% CI 0.70-0.96) compared with those who remained ALD.

Conclusions: Changes in SLD subtype classification are associated with distinct MALO risks.

Conflict of interest: Yes, NIH T32 DK007740

Association of changes in steatotic liver disease subtype classification with major adverse liver outcomes

Table. Association of changes in steatotic liver disease subtype classification with major adverse liver outcomes

Baseline	2-Year Landmark	No. (%)	Events	Person-Years	IR per 100 PY (95% CI)	Hazard Ratio (95% CI)*
MASLD	MASLD	194,635 (91.8)	3,418	799,771	0.43 (0.41-0.44)	1 [Reference]
	MetALD	15,720 (7.4)	431	63,561	0.68 (0.62-0.75)	1.55 (1.40-1.71)
	ALD	1,561 (0.7)	62	6,515	0.95 (0.74-1.22)	2.13 (1.66-2.74)
MetALD	MetALD	30,623 (65.8)	1,125	127,571	0.88 (0.83-0.93)	1 [Reference]
	MASLD	11,686 (25.1)	229	48,907	0.47 (0.41-0.53)	0.55 (0.48-0.64)
	ALD	4,236 (9.1)	279	16,976	1.64 (1.46-1.85)	1.80 (1.58-2.06)
ALD	ALD	4,260 (36.0)	272	16,639	1.63 (1.45-1.84)	1 [Reference]
	MASLD	1,325 (11.2)	28	5,692	0.49 (0.34-0.71)	0.31 (0.21-0.46)
	MetALD	6,256 (52.8)	335	25,391	1.32 (1.19-1.47)	0.82 (0.70-0.96)

ALD, alcohol-associated liver disease; CI, confidence interval; IR, incidence rate; MASLD, metabolic dysfunction-associated steatotic liver disease; MetALD, metabolic dysfunction and alcohol-associated liver disease; No, number; PY, person-years.

Note: Percentages have been rounded and may not total 100.

* Major adverse liver outcome was defined as the first occurrence of cirrhosis, decompensation, hepatocellular carcinoma, liver transplant, and liver-related death. Hazard ratios were estimated using cause-specific Cox proportional hazards regression models, adjusted for age, sex, smoking status, social deprivation index, and index year.

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ATORVASTATIN AND GENE EXPRESSION SIGNATURES IN HEPATOCARCINOGENESIS

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Introduction and Objectives: Hepatocellular carcinoma (HCC) represents a significant global health burden as the fourth leading cause of cancer-related deaths. While statins have shown promise in HCC prevention, their molecular mechanisms remain poorly understood.

We investigated the effect of atorvastatin (AT) on gene expression profiles and hepatocarcinogenesis in a hexachlorobenzene (HCB)-induced HCC model.

Materials and Methods: Male Wistar rats were divided into four groups: control, AT (5 mg/kg), HCB (100 mg/kg), and AT+HCB. After 30 days of treatment, we analyzed hepatosomatic index, liver histology, and performed RNA sequencing to evaluate transcriptomic changes. Gene Set Enrichment Analysis and KEGG pathway analysis were used to identify key molecular pathways. Protein expression of selected targets was confirmed by immunohistochemistry.

Results: HCB treatment significantly increased hepatosomatic index (28%, p<0.01) and induced preneoplastic lesions, which were

prevented by AT co-administration. RNA sequencing revealed HCB activated multiple oncogenic pathways, including RHO GTPase cycle, TGF- β , and receptor tyrosine kinase signaling, with 84.8% concordance with established cancer pathway genes. AT treatment upregulated protective PPAR signaling, autophagy, and cellular stress response pathways while downregulating oncogenic pathways activated by HCB. AT significantly reduced the expression of key oncogenic proteins including TGF- β 1, p53, and c-Myc in HCB-treated liver tissue.

Conclusions: Atorvastatin effectively prevents HCB-induced hepatocarcinogenesis through multiple mechanisms, including modulation of key oncogenic pathways and promotion of protective cellular responses. These findings provide new insights into the molecular mechanisms of statin-mediated HCC prevention and identify potential therapeutic targets for future interventions.

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REPRIORITIZING THE LIVER TRANSPLANT WAITING LIST: IMPACT OF AUTOMATIC MELD-NA 29 FOR REFRACTORY ASCITES

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Introduction and Objectives: In Brazil, liver allocation follows the MELD-Na score. To address high-risk conditions not reflected by high scores, special situations are evaluated individually. Refractory ascites and hepatocellular carcinoma (HCC) account for ~80% of such cases. In 2021, Technical Note No. 32/2021 granted 29 MELD-Na points to patients with refractory ascites to improve access to liver transplant (LT).

Primary, to compare the time from special situation approval to LT in cases of refractory ascites and HCC, before and after the new policy. Secondary, assess transplant volume and waiting list mortality in both groups.

Patients and Methods: Retrospective, single-center study including adult patients granted special situation for refractory ascites or HCC in 2018–2020 (pre-policy) and 2022–2024 (post-policy). Cases from 2021 were excluded. Outcomes were time to LT, mortality on the waiting list, and transplant numbers.

Results: In refractory ascites, median time to LT decreased by 95 days (186 to 91; –51.1%). In HCC, waiting time increased by 36 days (197 to 233; +18.3%). Waiting list mortality dropped in both groups: from 16% to 7% for refractory ascites and from 11% to 6% for HCC. The absolute number of transplants remained stable across periods.

Conclusions: Technical Note 32/2021 had a direct positive impact on patients with refractory ascites. However, it was associated with increased waiting time for HCC patients, although without increased mortality. These findings highlight the need for continuous monitoring of allocation policies and broader multicenter evaluation.

Conflict of interest: None

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