Immune Tolerant Hepatitis B: A Clinical Dilemma

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viruses

Review

Immune Tolerant Chronic Hepatitis B: The Unrecognized Risks

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Editorial

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The imitator of immune-tolerant chronic hepatitis B: A killer in disguise

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Keywords: Hepatitis B virus; Indolent immune clearance phase; Surveillance; Antiviral treatment; Liver biopsy

Conclusion

HBV infection is a perplexing and dynamic viral disease with a natural history that remains largely unpredictable to the clinician. Immune tolerant disease is best characterized by high viral replication in the setting of minimal liver inflammation and injury, and this stage can persist for decades. The risk of disease progression in the truly immune tolerant patient is believed to be low, but HCC risks are largely unknown and, again, unpredictable. We do not know whether current therapies will change the natural history of disease in these individuals, and whether we should commit these patients to long-term antiviral therapy—while enticing—is not yet a clinical question we can answer based on the currently available data. Many further studies are needed in this patient population.

JIM Original Article

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Elevated low-density lipoprotein cholesterol: An inverse marker of morbidity and mortality in patients with myocardial infarction

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Abstract. Schubert J, Lindahl B, Melhus H, Renlund H, Leosdottir M, Yari A, et al. Elevated low-density lipoprotein cholesterol: An inverse marker of morbidity and mortality in patients with myocardial infarction. *J Intern Med.* 2023;**OO**:1–12.

Background. The incidence of atherosclerotic cardiovascular disease increases with levels of low-density lipoprotein cholesterol (LDL-C). Yet, a paradox may exist where lower LDL-C levels at myocardial infarction (MI) are associated with poorer prognoses.

Objective. To assess the association between LDL-C levels at MI with risk factor burden and cause-specific outcomes.

Methods. Statin-naive patients hospitalized for a first MI and registered in SWEDEHEART were included. Data were linked to Swedish registers. Primary outcomes were all-cause mortality and nonfatal MI. Associations between LDL-C and outcomes were assessed using adjusted proportional hazards models.

Results. Among 63,168 patients (median age, 66 years), the median LDL-C level was 3.0 mmol/L (interquartile range 2.4–3.6). Patient age and comorbidities increased as LDL-C decreased. During a median follow-up of 4.5 years, 10,236 patients died, and 4973 had nonfatal MI. Patients with the highest LDL-C had a lower risk of mortality (hazard ratio [HR] 0.75; 95% confidence interval [CI] 0.71–0.80). The risk of hospitalization for pneumonia, hip fracture, chronic obstructive pulmonary disease, and new cancer diagnosis was lower with higher LDL-C (HR range, 0.40–0.81). Patients with the highest LDL-C had a greater risk of recurrent MI (HR 1.16; 95% CI 1.07–1.26).

Conclusions. Patients with the highest LDL-C levels at MI had the lowest incidence of mortality and morbidity. This seems to reflect lower age at MI, less underlying morbidities, paired with the modifiability of LDL-C. However, supporting the causal association between LDL-C and ischemic heart disease, elevated LDL-C was simultaneously associated with an increased risk of nonfatal MI.

Keywords: atherosclerosis, cholesterol, myocardial infarction, lipid lowering, observational, prevention

Conclusion

Patients with a first MI despite low LDL-C levels have increased risk of mortality and outcomes associated with ageing, compared with patients with higher LDL-C. Conversely, higher LDL-C was associated with an increased incidence of recurrent nonfatal MI. Further, a greater reduction in LDL-C after MI was associated with reduced mortality, even in those with the lowest LDL-C at the time of MI. These results indicate that there is no real paradox, rather that LDL-C is a marker of overall frailty reflecting morbidity and biological ageing and that patients who suffer an MI, despite low LDL-C, have other strong drivers of atherosclerotic CVD. This emphasizes the importance of continuing lipid-lowering treatment in patients with MI, regardless of the level of LDL-C at the time of that MI. This is of special significance when untreated LDL-C is low at the time of MI, as this might increase the risk of undertreating the patient.

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ARTICLE: LIVER

A Reappraisal of the Diagnostic Performance of B-Mode Ultrasonography for Mild Liver Steatosis

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accuracy, and area under the receiver operating characteristic curve (AUC).

RESULTS:

B-USG showed a sensitivity of 83.4%, specificity of 81.0%, and AUC of 0.822 in diagnosing mild liver steatosis (6.5% ≤MRI-PDFF ≤14%). The sensitivity, specificity, and AUC in diagnosing the presence of fatty liver disease (MRI-PDFF ≥6.5%) were 83.4%, 81.0%, and 0.822, respectively. The mean PDFF of B-USG–diagnosed nonfatty liver differed significantly from that of diagnosed mild liver steatosis (3.5% ± 2.8% vs 8.5% ± 5.0%, $P < 0.001$). The interinstitutional variability of B-USG in diagnosing fatty liver was similar in diagnostic accuracy among the 6 centers (range, 82.8%–88.6%, $P = 0.416$).

DISCUSSION:

B-USG was an effective, objective method to detect mild liver steatosis using MRI-PDFF as comparison, regardless of the etiologies and comorbidities.

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INVITED REVIEW

Alcohol and its associated liver carcinogenesis

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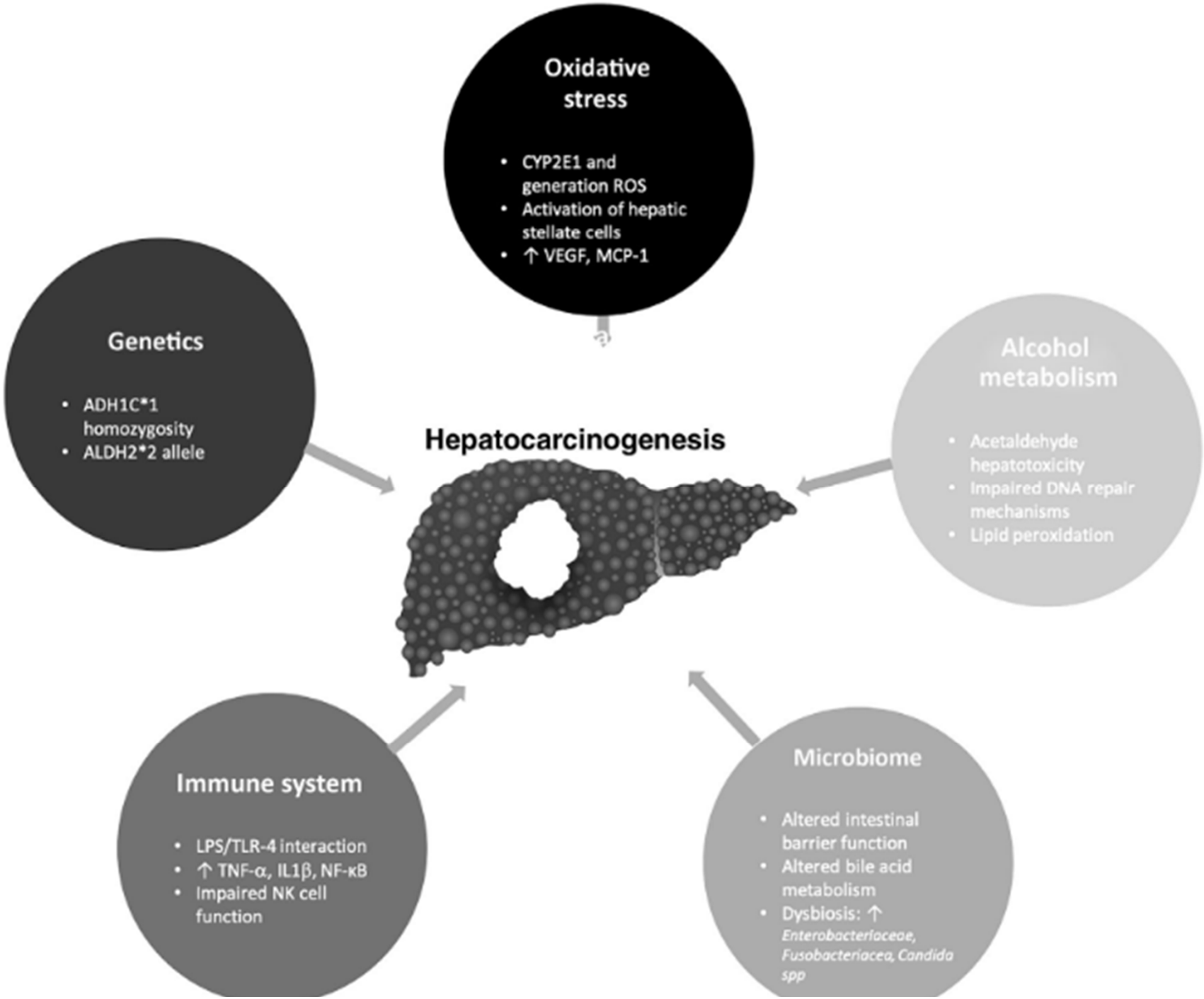
Abstract

Alcohol consumption is a major cause of cirrhosis and hepatocellular carcinoma (HCC). The prevalence of alcohol-associated hepatocellular carcinoma (aHCC) varies worldwide but is highest in Eastern Europe. Alcohol is the second fastest-growing cause of age-standardized liver cancer mortality with tumors more often diagnosed outside surveillance protocols and at a more advanced stage. Risk factors for aHCC include greater amounts of alcohol consumption, sex, and certain genetic polymorphisms. Smoking, concomitant liver disease, obesity, and diabetes act synergistically in increasing the risk of HCC in alcohol-associated liver disease. Alcohol-related hepatocarcinogenesis results from the complex interactions of several mechanistic pathways. Although not completely understood, underlying mechanisms include acetaldehyde-related hepatotoxicity, oxidative stress, activation of the innate immune system, and alterations of the host microbiome.


Oxidative stress
• CYP2E1 and generation ROS
• Activation of hepatic stellate cells
• ↑ VEGF, MCP-1
Genetics
• ADH1C*1 homozygosity
• ALDH2*2 allele
Hepatocarcinogenesis
Alcohol metabolism
• Acetaldehyde hepatotoxicity
• Impaired DNA repair mechanisms
• Lipid peroxidation
Immune system
• LPS/TLR-4 interaction
• ↑ TNF-α, IL1β, NF-κB
• Impaired NK cell function
Microbiome
• Altered intestinal barrier function
• Altered bile acid metabolism
• Dysbiosis: ↑ Enterobacteriaceae, Fusobacteriacea, Candida spp

Conclusions

aHCC is a heterogenous and often advanced disease due to the complex interplay of host risk factors. In view of the rising burden of ALD and aHCC, public health interventions are required to reduce alcohol consumption while also aiming to improve aHCC characteristics at diagnosis. Further research should focus on elucidating mechanisms of hepatocarcinogenesis further and novel therapeutic targets.

ORIGINAL ARTICLE

The combination of the enhanced liver fibrosis and FIB-4 scores to determine significant fibrosis in patients with nonalcoholic fatty liver disease

Zobair M. Younossi ✉, Maria Stepanova, Sean Felix, Thomas Jeffers, Elena Younossi, Zachary Goodman, Andrei Racila, Brian P. Lam, Linda Henry

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Results

There were 463 NAFLD patients included: 48 ± 13 years old, 31% male, 35% type 2 diabetes; 39% had significant fibrosis; mean ELF score was 9.0 ± 1.2, mean FIB-4 score was 1.22 ± 1.05. Patients with significant fibrosis were older, more commonly male, had lower BMI but more components of metabolic syndrome, higher ELF and FIB-4 ($p < 0.0001$). The performance of the two NITs in identifying significant fibrosis was: AUC (95% CI) = 0.78 (0.74–0.82) for ELF, 0.79 (0.75–0.83) for FIB-4. The combination of ELF score ≥9.8 and FIB-4 ≥ 1.96 returned a positive predictive value of 95% which can reliably rule in significant fibrosis (sensitivity 22%, specificity >99%), while an ELF score ≤7.7 or FIB-4 ≤ 0.30 had a negative predictive value of 95% ruling out significant fibrosis (sensitivity 98%, specificity 22%).

Conclusions

The combination of ELF and FIB-4 may provide practitioners with easily obtained information to risk stratify patients with NAFLD who could be referred to specialists or for enrollment in clinical trials.

THE END