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Abbreviations: AASLD: American Association for the Study of Liver Diseases;

AC: alcohol-related cirrhosis;

AH: alcoholic hepatitis;

ALD: alcohol-related liver disease;

AUD: alcohol use disorder;

AUDIT: Alcohol Use Disorders Identification Test

DSM: Diagnostic and Statistics Manual

EASL: European association for the study of the liver
LT: liver transplantation
MDF: Maddrey Discriminant Function
MELD: model for end-stage liver disease
NAFLD: non-alcoholic fatty liver disorder; NASH: non-alcoholic steatohepatitis;
NIAAA: National Institutes on Alcohol Abuse and Alcoholism
STOPAH: Steroids or pentoxifylline for alcoholic hepatitis

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The previous American Association for the Study of Liver Diseases (AASLD) practice guideline on 'alcoholic liver disease' published in 2010, has been an undoubted success (1). According to Google Scholar on June 14, 2019, it has received more than 1,400 citations. In 2018, the AASLD Practice Guideline Committee decided that the field was ready for a new guideline, now called 'a guidance'. We are the authors of the new guidance published in Hepatology (2). In this brief review, we will summarize the new document and draw attention to the areas of change and controversy. '***Guidance Statements'*** are shown in bold***.***

The new guidance is thematically different from the 2010 manuscript in that it places a heightened focus on alcohol use disorder (AUD) as the core feature of all alcohol-related liver disease (ALD). We have learnt from our colleagues in the world of addiction medicine of the negative role that stigma plays in exacerbating illnesses caused by excessive drinking. This recognition starts with the nomenclature adopted by

the American Psychiatric Association in the most recent iteration of the Diagnostic and Statistics Manual (DSM) that dropped the term alcoholism in favor of AUD (3). Likewise, we have adopted the terms alcohol-related liver disease and alcohol-related cirrhosis while keeping the acronyms ALD and AC, respectively. We have retained alcoholic hepatitis because of common usage, but this, in time, may also fall out of use. These changes parallel those suggested by the most recent European Association for the Study of Liver Diseases (EASL) guideline (4).

A focus on the nexus of AUD and ALD in our patient population is fundamental to all our sections, beginning with screening for and diagnosis of AUD, and the use of biomarkers of alcohol consumption. Thus, the first guidance statements are as follows:

- **All patients receiving care in primary care and gastroenterology/hepatology outpatient clinics, emergency departments, and inpatient admissions should be routinely screened for alcohol use using validated questionnaires.**
- **Brief intervention, pharmacotherapy, and referral to treatment should be offered to patients engaged in hazardous drinking (AUDIT-C ≥4, AUDIT >8, binge drinkers)**
- **Alcohol biomarkers can be used to aid in diagnosis and support recovery. Urine and hair ethyl glucuronide, urine ethyl sulfate, and phosphatidylethanol are not affected by liver disease, and therefore preferable.**

As in the previous guideline, abstinence from alcohol is the *sine qua non* of all treatment of AUD in patients with ALD. Heretofore, hepatologists and advanced practice providers (nurse practitioners and physician assistants) working in hepatology practices have not had the skill set to offer sophisticated assessment of and care for patients with ALD in combination with AUD. We believe that this is changing, through the adoption of a multidisciplinary approach to management of AUD, particularly with embedded addiction specialists in the clinic (5). Consequently, our guidance reflects this new reality as follows:

- **Referral to AUD treatment professionals is recommended for patients with ALD and/or AUD in order to ensure access to the full range of AUD treatment options.**
- **Multidisciplinary, integrated management of ALD and AUD is recommended and improves rates of alcohol abstinence amongst ALD patients.**
- **Based on limited data, the use of acamprosate or baclofen can be considered for the treatment of AUD in patients with ALD.**

Finally in relation to AUD, we offer specific guidance about drinking alcohol for patients, both with and without liver disease:

- **Patients without liver disease should be educated about safe levels of alcohol consumption for men (no more than 2 standard drinks per 24 hours) and women (no more than 1 standard drink per 24 hours).**
- **Patients with ALD or other liver diseases, in particular NAFLD, NASH, viral hepatitis, and hemochromatosis, should be counseled that there is no safe level of drinking, and that they should abstain.**

Several more specific areas of change and controversy are considered in the new guidance, such as the characterization of the clinical forms of ALD, consideration of the methods for the diagnosis of ALD including the role of liver biopsy, and clarification of the definitions AH and alcoholic steatohepatitis and acute on chronic liver failure (ACLF) in ALD (6). The management of patients with severe AH remains controversial. Unfortunately, the past decade has not provided breakthrough advances in the medical management of AH, other than confirming the value of abstinence. However, our knowledge base has been enhanced by the STOPAH trial in the United Kingdom, which has clarified the limited role of corticosteroids, and by the Lille score, which has improved stopping rules for corticosteroids (7,8). Our guidance for management of AH are:

- **The clinical diagnosis of AH (definite, probable, possible) should be made using the published consensus criteria**

- **Lab-based prognostic scores should be used to determine prognosis in alcoholic hepatitis.**
- **The Maddrey Discriminant Function (MDF) (≥32) should be used to assess the need for treatment with corticosteroids or other medical therapies.**
- **A MELD score >20 also should prompt consideration of corticosteroid treatment.**
- **Abstinence from alcohol should be promoted to improve long-term prognosis in AH.**
- **Prednisolone 40mg/day given orally should be considered to improve 28-day mortality in patients with severe AH (MDF ≥32) without contraindications to the use of corticosteroids.**
- **The addition of intravenous NAC to prednisolone 40 mg/day may improve the 30-day survival of patients with severe AH.**
- **The Lille score should be used to reassess prognosis, identify non-responders and guide treatment course after 7 days of corticosteroids.**
- **Patients with AH should have malnutrition addressed and treated, preferably with enteral nutrition.**
- **Pentoxifylline is no longer recommended in the treatment of AH.**

The 2010 AASLD guideline on ALD concluded with a short section on liver transplantation (LT) which, while acknowledging that LT was appropriate in carefully selected ALD subjects, also stated that a 6-month period of abstinence was recommended as a prerequisite to placement on the LT waiting list. The latter statement precluded LT as a treatment of life-threatening AH not responding to medical management. Since then, a prospective European pilot study, and a retrospective multicenter American study have shown good to excellent early results of LT in selected patients with life-threatening AH and recent alcohol use (9,10). We are still in the early stages of understanding how best to apply LT in patients with AH, and many unanswered questions remain about patient selection, treatment of AUD after LT, and longer term outcomes. In this fluid situation, we made the following guidance statements:

- **Patients with decompensated alcohol-related cirrhosis, Child-Turcotte-Pugh C or MELD-Na ≥21 should be referred and considered for LT.**
- **Candidate selection for LT in alcohol-related cirrhosis should not be solely based on a fixed interval of abstinence.**
- **LT may be considered in carefully selected patients with favorable psychosocial profiles in severe AH not responding to medical therapy.**

Finally, our document looks to the future and identifies the gaps in our knowledge which are ripe for further study:

1. Studies providing the accurate assessment of the prevalence of ALD, particularly identifying earlier, asymptomatic stages of ALD such as alcohol-related steatosis or moderate AH, are needed, and may become feasible with broader use of noninvasive steatosis and fibrosis assessment tools.
2. Well-constructed studies of the incidence of alcoholic hepatitis in the US are needed. Particular attention should be paid to diversity of sex, racial background and age.
3. ALD patients have been omitted from studies of efficacy of treatments for AUD. Studies are needed to assess the efficacy of psychosocial and pharmacological treatments in initiating and maintaining abstinence by patients with ALD.
4. The potential for serial measurements of biomarkers in patients with ALD are needed, with the dual endpoints of abstinence and stabilization or improvement in liver disease.
5. Studies of medical agents that abrogate the pathophysiological mechanisms that lead to chronic alcohol-related liver injury are needed. These processes include chronic inflammation, the role of the gut microbiota, progressive fat accumulation, and progressive fibrotic injury.
6. New clinical trials are needed both in moderate (MELD ≤20) and severe AH (MELD> 20) to improve the management of AH.
7. Prospective clinical studies of the utility of LT in selected patients with severe AH are needed. In particular, areas for investigation include processes of patient

selection, monitoring alcohol use before and after LT and treatment of AUD before and after LT.

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