



Review Article



Alcoholic Liver Disease in China: A Disease Influenced by Complex Social Factors That Should Not Be Neglected

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Abstract

Alcoholic liver disease (ALD) encompasses liver damage caused by chronic, excessive alcohol consumption. It manifests initially as marked hepatocellular steatosis and can progress to steatohepatitis, liver fibrosis, and cirrhosis. With China's rapid economic growth, coupled with a complex social background and the influence of a deleterious wine culture, the number of patients with ALD in China has increased significantly; the disease has become a social and health problem that cannot be ignored. In this review, we briefly described the social factors affecting ALD in China and elaborated on differences between alcoholic and other liver diseases in terms of complications (e.g., cirrhosis, upper gastrointestinal bleeding, hepatic encephalopathy, hepatocellular carcinoma, addiction, and other extrahepatic diseases). We also emphasized that ALD was more dangerous and difficult to treat than other liver diseases due to its complications, and that precise and effective treatment measures were lacking. In addition, we considered new ideas and treatment methods that may be generated in the future.

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Introduction

Alcoholic liver disease (ALD) is caused by chronic alcohol consumption and is among the most common causes of liver-related morbidity and mortality.¹ Its incidence is increasing worldwide, placing heavy burdens on healthcare systems.

ALD initially manifests as substantial hepatocyte steatosis, which can progress to steatohepatitis, liver fibrosis, and cirrhosis.² In the short term, severe alcoholism can also lead to acute severe alcoholic hepatitis, acute liver function damage, and even death. The underlying mechanism is complex, involving steatosis, inflammation, fibrosis, and carcinogenesis, and is the result of the combined effects of susceptibility genes, intestinal microecology, oxidative stress injury, immune injury, and programmed cell death.³ Despite tremendous progress in research on ALD, the pathogenesis of the disease remains unclear and effective therapies remain lacking. With the rapid growth of China's economy, the continuous opening up of its society, and the difficulty of solving the social problem of "wine culture", the number of people with ALD in China has increased considerably (currently exceeding 62 million), and ALD has become a public health problem that cannot be ignored. Taking the complex social context of China as a starting point, this review compares the characteristics of ALD (cirrhosis, upper gastrointestinal bleeding, hepatic encephalopathy, hepatocellular carcinoma, addictive nature, and related extrahepatic diseases) with those of other liver diseases. In addition, we identify problems with such comparisons and propose new treatment ideas and methods for the future.

ALD in the complex social context in China

ALD differs from some other diseases in that it is greatly influenced by social factors. The complex social context in China poses serious challenges related to ALD. For example, Chinese society has always relied on moral education in the management of underage drinking, whereas Western societies have explicitly prohibited the sale of alcohol to minors through regulations and laws. A large cross-sectional study published in 2016 indicated that alcohol use is prevalent among Chinese adolescents, with a current drinking rate of 7.3%. And 13.2% students reported having alcohol-related problems. The current data may be higher than before.⁴ Moreover, Chinese people are more inclined to drink spirits than other alcoholic beverages. The top five brands in the 2021 Global Alcohol Brands spirits ranking (Maotai, Wuliangye, Yanghe, Luzhou Laojiao, and Gujing Gongjiu) are widely known in China and hold very large shares of the market. Moreover, China's unbottled alcohol market accounts for nearly 20% of its national alcohol consumption

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market, whereas overseas alcohol markets have stricter regulatory constraints and more comprehensive rules. Unbottled alcoholic beverages in China are characterized by higher alcohol contents, complexity of ingredients, and insecurity of hygiene, and thus contribute to the incidence of ALD. In addition, the influence of China's uniquely deleterious wine culture exacerbates the current state of ALD in the country. Chinese businesspeople tend to negotiate and work together while playing drinking games, and the amount of alcohol consumed represents not only the sincerity of cooperation but also, to a certain extent, the establishment of public corporate relationships. Thus, businesspeople in China are encouraged to drink excessively, whereas those in Japan, for example, are not pressured to consume alcohol and do so purely voluntarily. According to a white paper published by the China Alcoholic Beverage Association, 60% of China's drinking population is "forced to drink". The proportion of regular drinkers among Chinese adults increased from 27.0% in 2000 to 66.2% in 2015, and the WHO also estimated that 22.7% of Chinese (aged 15+ years) had engaged in heavy episodic drinking in 2016.⁵ From 2005 to 2016, the per-capita consumption of pure alcohol among people aged ≥ 15 years in China increased by 76%; the most recent (2022) World Health Organization (WHO) statistical report provides an average value of 6.0 L, slightly above the global average of 5.8 L.⁶ In summary, we can infer that the burden of ALD in China is increasing gradually under the influence of a complex social background and a harmful alcohol consumption-based culture.

Current status of ALD

Status of ALD worldwide

Globally, 43% of the population currently consumes alcohol. Alcohol abuse has become a significant risk factor for disease, disability, and death worldwide.⁷⁻¹⁰ The global proportions of deaths attributable to alcohol are 7.6% for men and 4.0% for women.¹¹ Alcohol-related diseases of different organs and injuries caused by traffic accidents and violence result in 3.3 million deaths (5.9% of all deaths) per year.¹² Alcohol-related harms particularly affect working-aged people, with 139 million disability-adjusted life years (DALYs) lost due to alcohol consumption, representing 5.1% of the total global burden of disease.¹³ The global incidence of alcohol-related hepatitis has increased in recent years, especially among young people and women.¹⁴ Alcohol is among the most common causes of end-stage liver disease, and it is implicated directly or indirectly in 50% of cirrhosis-related deaths.¹⁵ Worldwide, ALD accounts for 4% of deaths and 5% of DALYs lost.¹⁶ One in 10 alcohol-related deaths is due to alcohol-related cirrhosis of the liver, and nearly 50% of alcohol-related deaths are due to liver disease, equating to 225,000 DALYs lost per year.¹⁷ According to the Global Burden of Disease study, an estimated 256,900 people died of cirrhosis and chronic liver disease in 2016, and 334,900 (27%) of these deaths were attributed to alcohol.¹⁸ In addition, 245,000 people died of alcohol-related hepatocellular carcinoma (HCC), accounting for 30% of all HCC deaths.¹⁹ In America, the proportion of cirrhosis cases due to alcohol consumption increased from 28% to 33% in past 10 years. And in Germany of 2018, alcohol consumption remained the dominant cause of cirrhosis, accounting for 52% of cirrhosis cases.²⁰

Status of ALD in China

Over the past 30 years, as the Chinese economy has continued to grow, overall alcohol consumption has increased

and the status of ALD has become more severe. In China, alcohol use disorders (AUDs), which include harmful drinking patterns such as alcohol dependence and abuse, commonly develop into conditions associated with physical and mental health problems and social dysfunction. The proportion of individuals with AUDs increased dramatically from 0.45% in the mid-1980s to 3.4% in the mid-1990s, with a lifetime prevalence of 9% from 2001 to 2005.²¹ Data from China in 2019 showed that alcohol consumption is a major contributor to the total disease burden, where it was the eighth-greatest contributor to disability-adjusted life-years lost.²² According to data from the Liver Disease Center of the Chinese People's Liberation Army's 302 Hospital, the proportion of patients hospitalized for ALD increased from 1.7% in 2002 to 4.6% in 2013.²³ Alcohol consumption is increasing steadily in China, faster than in other countries; China is currently among the largest per-capita consumers of pure alcohol worldwide.²⁴ As a result, the prevalence of ALD in China (4.5%) is now comparable to that in the United States (6.2%) and European countries (6%), and higher than that in Japan (1.56–2.34%).²⁵⁻²⁷ A meta-analysis of integrated epidemiological studies of ALD in Asia from 2000 to 2020 showed that liver cirrhosis attributed to alcohol was 12.57%. In HCC, the proportion was 8.30%.²⁸ The status of ALD in China is thus serious and requires increased attention.

Why ALD should be taken seriously?

ALD differs from other liver diseases

ALD encompasses alcoholic fatty liver disease, alcoholic hepatitis, steatohepatitis, liver fibrosis, cirrhosis, and liver cancer.²⁹ The underlying mechanism is complex, involving steatosis, inflammation, fibrosis, and carcinogenesis, and is the result of the combined effects of susceptibility genes, intestinal microecology, oxygen stress injury, immune injury, and programmed cell death. The early stage of ALD is characterized by fat accumulation in the liver and is the only stage of the disease that can be completely reversed by abstinence without drug intervention.³⁰ Clinically, in contrast to patients with other liver diseases, those with ALD are often characterized by combined multisystemic injury and poor compliance (Fig. 1). In addition, alcohol is a significant driver of death among patients with liver diseases or other etiologies.

Cirrhosis

In recent years, the incidence of alcoholic cirrhosis has increased due to the rise in alcohol consumption in China. Alcoholic cirrhosis begins with the accumulation of fat in the liver, resulting in conditions such as steatosis and inflammation, which then develop into fibrosis and eventually lead to the degradation of the normal liver structure, culminating in irreversible disease.¹³ As many patients with alcoholic cirrhosis experience symptoms and complications related to alcohol overuse, the disease is often diagnosed secondary to other conditions, such as alcoholic hepatitis with jaundice, anemia or electrolyte imbalance, pancreatitis, and infection.³¹ Fibrosis is a prerequisite for the development of cirrhosis. The liver promotes hepatic fibrosis in response to alcohol through various mechanisms, such as the ethanol metabolite acetaldehyde-induced secretion of transforming growth factor- β ,^{32,33} lipopolysaccharide-induced activation of hematopoietic stem cells (HSCs) by activated Kupffer cells, acetaldehyde-promoted collagen production and deposition, HSC activation by activated Kupffer cells through a variety of profibrotic mediators,³⁴ reduction of metalloproteinase activity by reac-

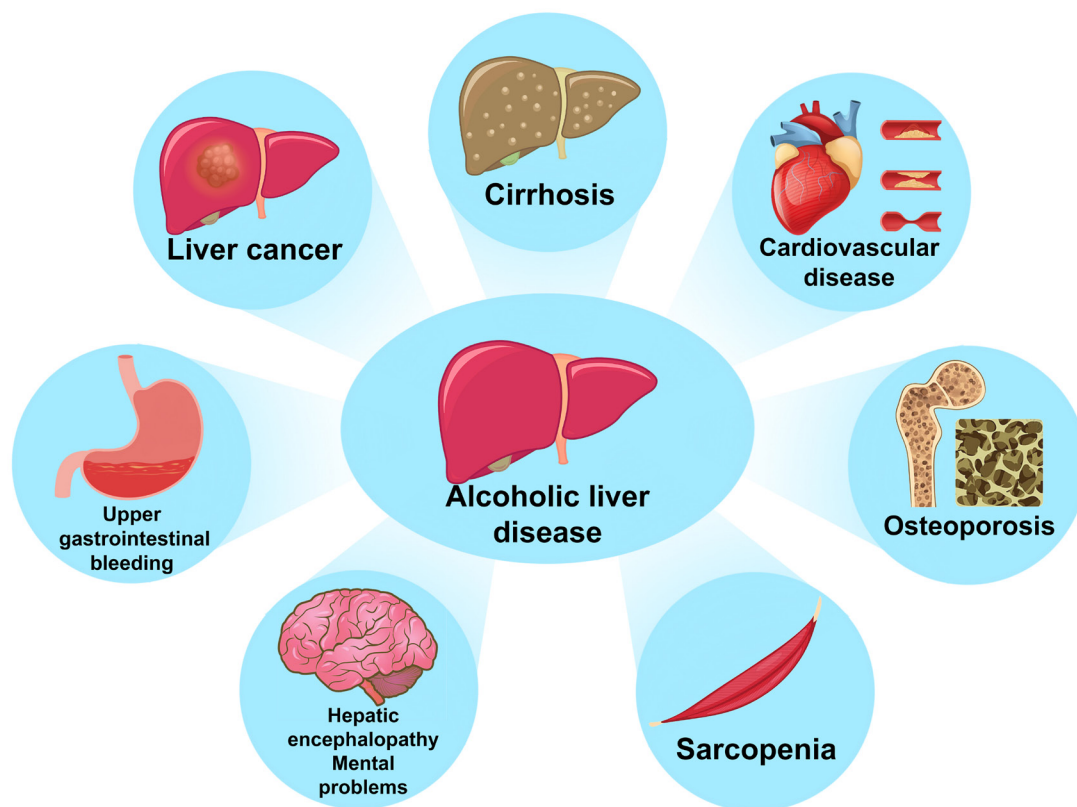


Fig. 1. Complications associated with alcoholic liver disease.

tive oxygen species (ROS) leading to collagen accumulation, stimulation of profibrotic HSC signaling pathways (extracellular regulated protein kinase, phosphatidylinositol 3 kinase/protein kinase B, and c-Jun N-terminal kinase) generation by ROS,³⁵ and production of profibrotic factors upon hepatocyte apoptosis.^{36,37}

Approximately 2 billion people consume alcohol and 75 million people are diagnosed with AUDs and are at risk of alcohol-associated liver disease worldwide. Cirrhosis is currently the 11th most common cause of death globally, leading to 1.16 million deaths per year, and is among the top 20 causes of DALYs and years of life lost, accounting for 1.6% and 2.1%, respectively, of the global burden.³⁵ Eleven percent of all cirrhosis deaths occur in China.³⁸ The incidence of alcoholic cirrhosis is 10-fold greater among people with excessive alcohol use than in the non-drinking general population. The incidence rates of alcoholic liver cirrhosis among men and in the general population were 50 and 4.8 per 10,000 person-years, respectively; the equivalent rates among women were 42 and 2.3 per 10,000 person-years, respectively.³⁹ More than 50% of deaths associated with cirrhosis worldwide are attributable to alcohol.¹⁵ The incidence of cirrhosis is greater in patients with ALD than in those with nonalcoholic fatty liver disease, Buga syndrome, hepatomegaly, and drug- or chemical toxicity-related cirrhosis.⁴⁰ In terms of complications, patients with alcoholic cirrhosis have significantly greater incidences of palmar erythema, spider angioma, combined ascites, and jaundice than do patients with post-hepatitis B cirrhosis.⁴¹ In addition, aspartate transaminase/alanine transaminase ratios, which reflect liver cell damage and decreased liver function, are significantly higher in patients with alcoholic cirrhosis than in those with

post-hepatitis B cirrhosis. The research of single-cell RNA transcriptomics showed that, the patients with alcoholic cirrhosis have increased ratio of intrahepatic monocyte/macrophages and a dysfunctional adaptive immune response in the liver than those with HBV-induced cirrhosis. Suggesting that the former have severe cellular and humoral immunoregulation imbalances.⁴²

Upper gastrointestinal bleeding

The incidence of upper gastrointestinal bleeding may be greater in patients with ALD than in those with other liver diseases due to gastric mucosal damage, portal hypertension, and gastroduodenal ulcers resulting from alcohol consumption.⁴³ Liver function continues to deteriorate in patients with ALD when cirrhosis progresses to the decompensated phase relative to that in patients with average cirrhosis. Alcohol consumption leads to the impairment of plasminogen synthesis and prolonged prothrombin times, causing declines in platelet and coagulation function and increasing the likelihood of acute hemorrhage development in the digestive tract.⁴⁴ Moreover, patients with alcoholic cirrhosis are more likely to develop abdominal wall varices than those with post-hepatitis B cirrhosis, possibly because alcohol acts on stellate cells in the perisinusoidal space, leading to increased resistance to blood flow in the sinusoids, which is likely to lead to upper gastrointestinal hemorrhage after alcohol abuse.⁴⁵ Patients with gastrointestinal diseases who drink alcohol are more likely than those who do not drink alcohol to experience upper-gastrointestinal-tract bleeding due to the destructive effect of ethanol on the gastric mucous membrane barrier, which exacerbates the existing gastrointestinal disease and subsequently has an erosive effect on blood ves-

sels.⁴⁶ A survey showed that the proportion of upper gastrointestinal bleeding caused by the rupture of esophageal and fundal varices due to alcoholic cirrhosis was greater than that caused by cirrhosis due to other factors (e.g., cryptogenic, autoimmune, pharmacological, and biliary) (24.5% vs. 15.4%).⁴⁷ Moreover, alcohol consumption was found to induce more upper-gastrointestinal-tract bleeding (23.5%) than did medication use (5.9%), poor diet (8.8%), and other factors (5.9%) in a group of young people.⁴⁷ Thus, the evaluation of a patient with suspected upper-gastrointestinal-tract bleeding should begin with a thorough history of the patient's medication use and social factors (alcohol, tobacco, and substance use) and physical examination.⁴⁵

Hepatic encephalopathy

Prolonged alcohol consumption can cause silent changes in the structure and function of the central and peripheral nervous systems, increasing the likelihood of developing various encephalopathies.⁴⁸ Patients with ALD have impaired liver function and a reduced ability to synthesize urea, impairing their ability to eliminate potentially toxic levels of nitrogen-containing substances, ultimately leading to an increased risk of hepatic encephalopathy.⁴⁹ The incidence of hepatic encephalopathy as a complication was found to be greater among patients with severe alcoholic hepatitis (26.1%) than among those with gastrointestinal bleeding (21.7%) and acute kidney injury (9.9%).⁵⁰ Among patients with hepatic encephalopathy, the mortality rate is significantly higher among those with histories of alcohol consumption compared to those without, and the mortality rate due to alcoholic cirrhosis (25%) is greater than that due to post-hepatitis B cirrhosis (12.7%).⁵¹ Comparing with other liver diseases, patients with alcoholic cirrhosis had the highest risk of hepatic encephalopathy. The 1-year and 10-years cumulative HE incidences were 6.4% and 26%.⁵² A survey showed that the incidence of hepatic encephalopathy was significantly higher and the improvement rate significantly lower among patients with alcoholic cirrhosis than among those with post-hepatitis cirrhosis.⁵³ The diagnosis of hepatic encephalopathy, whether clinically evident or not, requires clinical skill, as the disease's clinical symptoms and neuropsychological and neurophysiological manifestations are nonspecific. Thus, the diagnosis can be made only after other possible causes of brain dysfunction have been ruled out.⁵⁴

Liver cancer

In 2020, the incidence rate of primary liver cancer ranked fifth among those for malignant tumors in China, with 410,000 new cases diagnosed, and the death rate ranked second, with 391,000 deaths recorded.⁵⁵ Risk factors for liver cancer include hepatitis B and C infection, fatty liver disease, alcohol-related cirrhosis, smoking, obesity, diabetes mellitus, iron overload, and various dietary exposures. At present, alcohol is believed to cause HCC through three main mechanisms.⁵⁶ First, long-term alcohol consumption reduces the detoxification function of the liver, nutrient intake, and the body's immunity. Second, acetaldehyde, an intermediate metabolite of alcohol, is thought to promote HCC development. Third, heavy drinking may lead to alcoholic cirrhosis, which may progress to HCC.⁵⁷ The most common cause of HCC is alcohol consumption (accounting for 32–45% of cases).⁵⁸ Of all alcohol-induced deaths from malignant tumors, 80,600 [23.9%; 14,800 (16.2%) among women and 65,900 (26.8%) among men] were caused by liver cancer. Liver cancer deaths attributable to alcohol consumption were

responsible for 0.2% of all deaths (0.1% among women and 0.2% among men), 10.7% of deaths from liver cancer (6.4% among women and 12.7% among men), and 1.7% of all alcohol-attributable deaths (0.9% among women and 2.1% among men).⁵⁹ Of the DALYs lost due to malignant neoplasms attributable to alcohol consumption, 2,142,000 [24.7%; 335,000 (14.9%) among women and 1,807,000 (28.2) among men] were caused by liver cancer, representing 11.2% (6.4% among women and 13.0% among men) of DALYs lost due to liver cancer. A 2.4-fold greater risk of liver cancer has been reported for individuals who drink more than one but not more than two alcoholic beverages per day on average than for individuals who do not drink alcohol, and a 3.8-fold greater relative risk has been reported for those who consume more than two alcoholic beverages per day.⁶⁰ Patients with alcohol-associated HCC usually develop the disease at a younger age and have poorer liver function and prognoses than do those with other nonviral-associated forms of HCC. Moreover, the rates of intra- and extrahepatic tumor metastasis are greater among patients with alcohol-associated HCC than among those with hepatitis B-associated HCC.⁶¹ This HCC is usually diagnosed as a more advanced stage and consequently with a lower survival rate.⁶² Bucci *et al.*⁶³ reported that the median overall survival time was significantly shorter for patients with alcohol-associated HCC than for those with hepatitis C-associated HCC (27.4 vs. 33.6 months).

Addiction

Alcohol addiction is characterized by psychological and somatic dependence and withdrawal syndrome. Psychological dependence involves strong, uncontrollable alcohol cravings, while somatic dependence reflects biological changes in the central nervous system due to repeated alcohol consumption over long periods. A series of withdrawal symptoms occur when alcohol consumption is terminated or abruptly reduced and can only be alleviated by the repeated use of alcohol or pharmacologically similar substances.⁶⁴ Alcohol addiction has become a major risk factor for death and disability, affecting approximately 4% of the global adult population.²⁷ A WHO survey indicated that 3.8% of the 2 billion people worldwide who consume alcoholic beverages are diagnosed with alcohol addiction.⁶⁵ In China, for males the prevalence of alcohol dependence, alcohol abuse were 4.4% and 4.0%; the corresponding values for females were all below 0.2, 0.1.⁶⁶ Long-term alcohol consumption can cause organic brain damage resulting in personality disorders, pronounced impulsive tendencies, poor self-control, family conflict, and interpersonal tension. Moreover, alcoholic patients who have been hospitalized are prone to experience negative emotional states after discharge, which greatly facilitates the resumption of drinking, leading to a high relapse rate and representing a major challenge in the clinical treatment of alcohol addiction.⁶⁷ Relapse rates of 60–70% at 3 months and 80–90% at 1 year after treatment have been reported for individuals with alcohol dependence.⁶⁸ Abstinence from alcohol is often the first step in the treatment of ALD and is greatly complicated by alcohol addiction.

Other related extrahepatic diseases

The prevalence and severity of sarcopenia are usually greater among patients with ALD than among those with other liver diseases, such as metabolism-related fatty liver disease and viral hepatitis.^{69,70} Sarcopenia can occur at all stages of ALD, and its severity depends on the severity of liver disease and extent of alcohol consumption.⁷¹ Available data indicate that 60–70% of patients with ALD have some de-

gree of sarcopenia.^{69,72} In addition, ALD has different effects on bone density at various skeletal sites.⁷³ A large cohort study showed that hip fractures occurred five times more frequently in patients with ALD than in other patients.⁷⁴ In addition, patients with ALD are more likely than those with chronic viral hepatitis to develop osteoporosis or bone loss.⁷⁵ Moreover, the risk of cardiovascular disease is significantly increased among patients with alcohol addiction⁷⁶ and persistent heavy alcohol consumption significantly increases the risk of ischemic stroke.⁷⁷

ALD is both a medical and social problem

The irrational consumption of alcohol contributes not only to the growing burden of ALD and the increased need for medical care, but also to a societal burden. Alcohol consumption is strongly correlated with violent crime, and positively associated with fatal acts of violence in some regions.^{78–80} In addition, drunk driving and accidental deaths occurring under the influence of alcohol pose significant burdens on society. In Latin America, approximately 30% of road fatalities are attributable to alcohol; and the burden of road crashes overall represented 1.5–3.9% of the gross domestic product in 2013, compared with approximately 2% in the USA.^{81,82} Similarly, in China in 2015, approximately 30% of road traffic deaths, or 93,750 fatalities, were attributed to drunk driving,⁸³ and the offense has replaced theft as the most commonly prosecuted crime.⁸⁴ Thus, drunk driving not only consumes many social resources, but also deprives society of a significant amount of labor, thereby having a considerable societal impact.

Treatment strategies

Current ALD treatment strategies and dilemmas

According to the Guidelines for the Management of Alcoholic Liver Disease published by the Chinese Medical Association's Liver Disease Branch in 2018,⁸⁵ the principles of ALD treatment include abstinence from alcohol, nutritional support, reduction of disease severity, improvement of preexisting secondary malnutrition, and symptomatic treatment of alcoholic cirrhosis and its complications. Complete abstinence from alcohol is the primary and most basic ALD treatment, but achieving it is difficult due to alcohol addiction in people with the disease, and supporting medication may be needed. The importance of nutritional support reflects the common occurrence of malnutrition among patients with ALD and its correlation with the severity of the disease.⁸⁶ While some glucocorticosteroids and other drugs are used for ALD treatment, their therapeutic effects are unsatisfactory and vary among patients. Liver transplantation may be an option for patients who do not respond well to medication, but it is not always effective due to the limited supply of organs and the possible occurrence of post-transplantation complications. ALD treatment guidelines from China, the United States, and Europe differ in several respects. For example, China's guidelines require patients with ALD who are undergoing liver transplantation to abstain from alcohol for 3–6 months before the procedure and to have no serious alcohol-induced injury to other organs. In contrast, the European Association for the Study of the Liver (EASL) and American College of Gastroenterology (ACG) guidelines suggest that 6 months of abstinence from alcohol should no longer be considered as a requirement for transplantation because patients with severe or end-stage disease may die before achieving such abstinence.⁸⁷ In addition, while the Chinese guidelines indicate that glucocorticosteroids im-

prove the survival rate of patients with subarachnoid hemorrhage at 28 days (but have no obvious effect at 90 days or 6 months), the EASL and ACG guidelines give clearer indications for hormone therapy, including hormone types, dosages, treatment durations, and treatment responses. The Chinese guidelines also mention various drugs, such as metadoxine and S-adenosylmethionine, for which additional evidence is needed.⁸⁷ Regional ALD guidelines need to be developed based on evidence-based medicine and population characteristics.

Future solutions

Regulation of drinking behavior

The WHO has led a series of initiatives to reduce alcohol consumption worldwide, three of which are considered to be the most cost-effective policies: taxation, supply reduction, and restrictions on promotion. Alcohol consumption can be further reduced by regulating the hours of sale, controlling the issuance of alcohol licenses, and establishing a legal age of purchase, among other measures.²⁰ China has not taken such measures, and their implementation can be considered from the perspective of government legislation.

Intestinal probiotic therapy

The gut microbial community is closely associated with ALD and is involved in pathological processes such as hepatocellular steatosis, steatohepatitis, liver fibrosis, cirrhosis, and HCC.⁸⁸ Growing evidence indicates that alcohol intake leads to major changes in the gut microbial composition and the loss of gut barrier function, thereby accelerating the progression of alcohol-induced liver injury.⁸⁹ In recent years, probiotics have been found to have protective and palliative effects on various complications of ALD, and many approaches have been explored to modulate and restore the gut microbiota in patients with ALD and improve microbiota–gut–liver–brain axis communication as a way of decreasing alcohol intake and slowing the progression of the disease.⁹⁰ The future development of novel probiotic strains and related products will hopefully provide additional options for the treatment of different stages of ALD. The effectiveness and safety of new probiotic preparations will need to be confirmed.

Traditional Chinese medicine

Many traditional Chinese medicine scholars, who have adopted holistic concepts of diagnosis and treatment and base medicinal prescription on their own clinical experience and rationale, have reported great benefits in the treatment of ALD. Natural traditional Chinese medicines play important roles in the treatment of this disease due to their multiple targets, potency, and low risk of side effects. Some traditional Chinese medicine monomers, their extracts, and combinations have been shown to effectively prevent the pathogenesis of ALD and to be useful in its treatment. For example, Qiu *et al.*⁹¹ reported that *Hovenia dulcis* extract ameliorated chronic alcoholic liver injury in rats, and Liu *et al.*⁹² reported that *Pueraria lobata* shows good efficacy in the initial treatment of ALD. In addition, clinical studies have shown that Zhi-Zi-Da-Huang decoction was effective in the treatment of ALD by antioxidant mechanism.⁹³ Other studies have shown that Xie-Zhuo-Tiao-Zhi formula can alleviate alcohol-induced liver injury, oxidative stress, and inflammation possibly through modulation of Nrf2/Keap1 and MAPKs/NF- κ B signaling pathways.⁹⁴ In the treatment of ALD, whether it is staged or based on type or evidence, traditional Chinese medicine thus has better effects. Tradi-

tional Chinese medicine can not only relieve patients' pain, but also improve their quality of life, and its use to treat ALD in the future would be a very promising direction.

Summary

Under the influence of many social factors, the number of Chinese patients with ALD is increasing annually. ALD has more complications than other liver diseases and is more dangerous. At present, China's system for the diagnosis and treatment of this disease is imperfect, and effective drugs and attention from doctors, patients, and society are lacking. Thus, additional research on ALD is needed.

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Conflict of interest

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Author contributions

Writing the original draft (XF, NH); review and editing (YW, XC); literature research (FG, CZ); and conceptualization and funding acquisition (TS, BZ). All authors have read and approved the final version of the manuscript.

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