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NONINVASIVE LIVER CIRRHOSIS: A FUTURE PROSPECTIVE

Pradyumna Kumar Behera*, Priyambada Rout and Debasish Pradhan

University Dept. of Pharmaceutical Sciences, Utkal University, Bhubaneswar-04, Odisha, India.

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***Corresponding Author**
Pradyumna Kumar Behera
University Dept. Of Pharmaceutical Sciences, Utkal University, Bhubaneswar-04, Odisha, India.

ABSTRACT

Cirrhosis is chronic injury to the liver from a variety of different sources can result in irreversible scarring of the liver. In developed countries, it is an increasing cause of morbidity and mortality & globally 14th most common cause of death. Among the major cause of chronic liver disease, chronic hepatitis C virus infection is foremost which leads to necroinflammation and fibrosis. Methods like predicting prognosis in patients with Liver Cirrhosis[1] have been developed for assessing liver fibrosis and have been used which are noninvasive. Liver Cirrhosis often have Protein Energy Malnutrition (PEM) and poor physical activity resulting in sarcopenia, which is the loss of skeletal muscle volume and increased muscle weakness.

From this review the current understanding of cirrhosis as a dynamic process and outline current therapeutic option for prevention and treatment of cirrhosis complication. By conducting rigourous clinical studies there is need for prevention of liver transplantation in more patients with cirrhosis in future.

INTRODUCTION

Chronic injury to the liver from a variety of different sources can result in irreversible scarring of the liver, known as cirrhosis. It results from different mechanisms of liver injury that leads to necroinflammation and fibrogenesis; histologically it is characterised by diffuse nodular regeneration surrounded by dense fibrotic septa with subsequent parenchymal extinction and collapse of liver structures, together causing pronounced distortion of hepatic vascular architecture. It is a major cause of morbidity and mortality in the USA, and according to the Centers for Disease Control and Prevention was responsible for 31,903

deaths in 2010 alone. It is thus of the utmost importance to manage these patients appropriately in the inpatient and outpatient setting to improve morbidity and mortality.

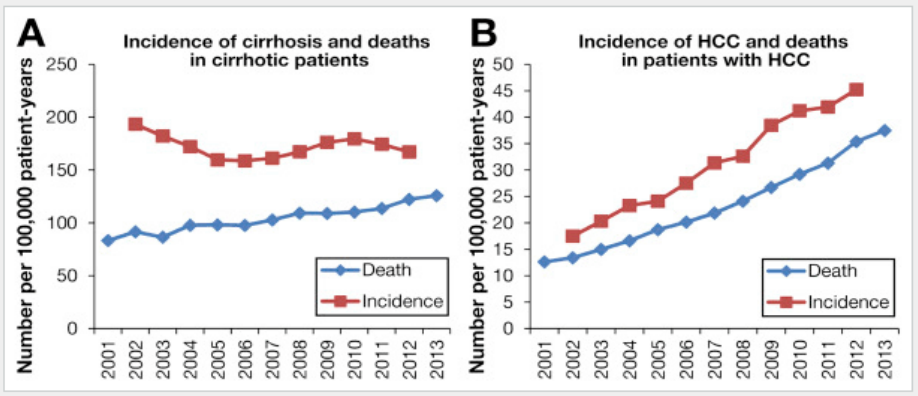


Figure 4

Trends in the incidence and mortality of cirrhosis and HCC between 2001 and 2013 in the VA health care system. HCC, hepatocellular carcinoma.

Cirrhosis is of two types;

1. Compensated cirrhosis:

*Function of the liver is well preserved.

*The underlying architecture is consistent with extensive fibrosis.

2. Decompensated cirrhosis:

*Developement of complications directly related to liver disease.

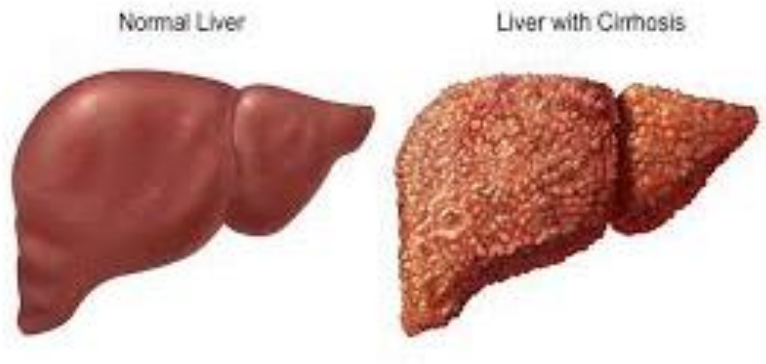
*Mortality rate begins to rise with the onset of decompensating episodes.

	Compensated Cirrhosis		Decompensated Cirrhosis	
Stage	Stage 1	Stage 2	Stage 3	Stage 4
Clinical	No Varices No Ascites	Varices No Ascites	Ascites +/- Varices	Bleeding +/- Ascites
Death (at 1 Year)	1%	3%	20%	57%

Malnutrition is common in end-stage liver disease (cirrhosis) and is often associated with a poor prognosis. Malnutrition occurs in all forms of cirrhosis as shown by studies of nutritional sta in cirrhosis of differing etiology and of varying degrees of liver insufficiency.

The prevalence of malnutrition in cirrhosis ranges from 65 to 100% depending upon the methods used for nutritional assessment and the severity of liver disease.

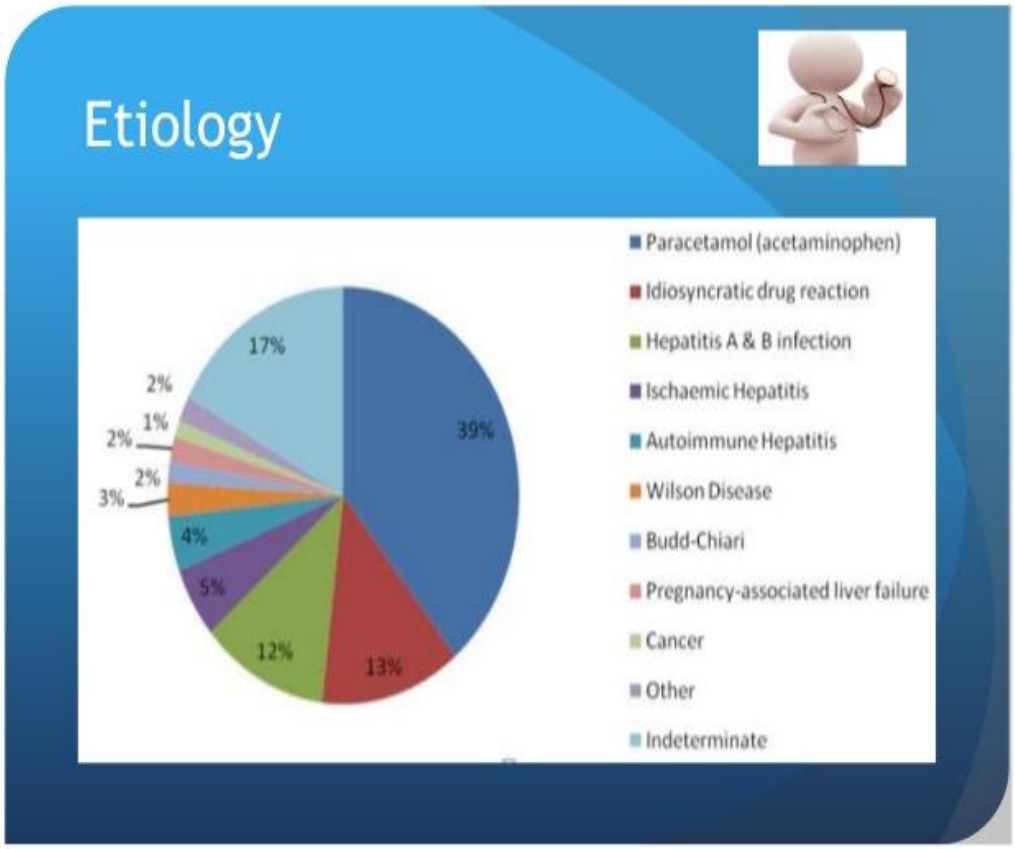
Clinically, cirrhosis has been regarded as an end-stage disease that invariably leads to death, unless liver transplantation is done, and the only preventive strategies have been screening for oesophageal varices and hepatocellular carsinoma.



The aim of the present review is to highlight the implications of malnutrition in patients with cirrhosis on disease outcome, on management of the central nervous system (CNS) complications of cirrhosis and on outcomes following liver transplantation. Nutritional recommendations are also formulated and some areas for future research needs are identified.

Etiology

Cirrhosis can arise in consequence of a toxic, infectious, allergic, immunopathological, or vascular process or an inborn error of metabolism. The commonest causes of cirrhosisin Germany are alcoholic and non-alcoholic fatty liver disease and viral hepatitis. Among these causes, the most common of all is alcoholic fatty liver disease, which caused 8619 deaths in Germany (8.9 deaths per 100 000 population) in 2009 and thus ranks among the country's top 20 causes of death. 0.5% of the German population are chronically infected with the hepatitis B virus, and 0.5% with the hepatitis C virus.



Diagnosis

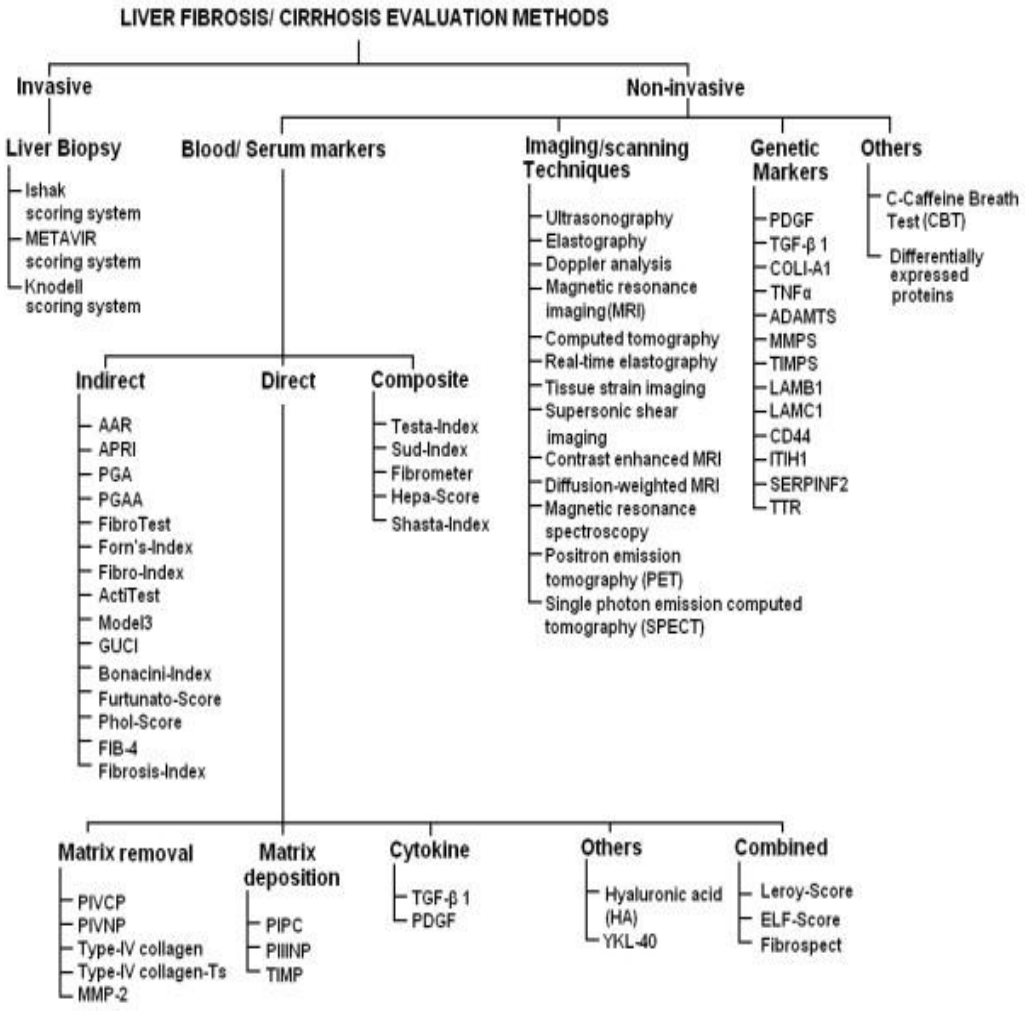
Cirrhosis is histologically characterized by fibrous septa between the portal fields; it comes in micro and macro-nodular forms. The condition is diagnosed by its characteristic findings on clinical examination, laboratory tests, and ancillary studies.

Cirrhosis can be diagnosed by;

1. Complete blood count test(CBC)
2. Liver function tests including alkaline phospatase, Serum glutamic pyruvic transaminase(SGPT)
3. Serum albumin
4. Liver biopsy
5. Liver scan
6. Upper GI barium swallow
7. Computed tomography(CT) of the abdomen
8. Magnetic resonance imaging(MRI) of the abdomen
9. Ultrasound of the abdomen

Noninvasive Methods for Predicting Liver Cirrhosis

Noninvasive markers of Liver Cirrhosis can be radiologic or serumbased. Although liver biopsy remains the reference standard for evaluating the extent of liver fibrosis in patients with chronic liver diseases, several noninvasive methods have been developed as alternatives to liver biopsies. Recent reports have focused on assessing the performance of noninvasive methods through long-term follow-up studies with clinical outcomes associated with Liver Cirrhosis.



Future therapies

Currently licensed drugs, such as non-selective β-blockers, statins, oral antibiotics, and anticoagulants are likely to be used in various combinations to prevent and treat complications of cirrhosis in the near future.[4,5] Statins reduce HVPG and are associated with reduced incidence of hepatocellular carcinoma. Anti coagulation used to be considered a contraindication in cirrhosis; however, stable cirrhosis is characterised by normal thrombin

generation and even hyper coagulability.[6] Currently, anticoagulation is considered only in patients with portal-vein thrombosis awaiting liver transplantation.[7] However, an RCT of enoxaparin in 70 patients with advanced cirrhosis showed that the drug was associated not only with lower risk of portal-vein thrombosis, but also with delayed decompensation and improved survival.[8] Confirmatory trials are needed before these findings can be translated into clinical practice. A surgically implanted pump transferring ascites to the bladder has been tested fore fractory ascites, but RCT evidence and safety data are needed.[9] Rifaximin is a potential alternative for prevention of spontaneous bacterial peritonitis since no bacterial resistance has been documented, and in observational studies HVPG and plasma endotoxin concentrations were lower with this treatment,[10] systemic haemodynamics and renal function also improved,[11] but these findings need confirmation. Metformin was independently associated with reduced incidence of hepatocellular carcinoma in a prospective cohort study of patients with hepatitis-C related cirrhosis[12] and in a case-control study of 97430 hepatocellular carcinoma patients,[13] the latter in a dose-dependent manner; this drug could have preventive properties in stage 1 or 2 cirrhosis.

CONCLUSIONS

Cirrhosis should no longer be considered as a single disease stage, because it has distinct clinical prognostic stages with substantial differences in 1-year survival. Clinicians should try to diagnose advanced liver disease as early as possible and to prevent the progression to further clinical stages and the advent of complications. We have previously reviewed the potential expansion of current indications of widely used drugs for preventing such complications. Strategies for population screening need to be tested aiming at early diagnosis of advanced fibrosis or high risk of progression. General lifestyle measures including alcohol and smoking cessation and weight loss should be advised, and every contact with health providers should be exploited for health education. Diagnosis before decompensation and implementation of these measures, as well as specific treatments when applicable, are important steps towards reducing the mortality of end-stage liver disease. All patients with decompensation should be closely monitored and followed up, because they might become candidates for liver transplantation depending on the course of their liver disease. The challenge in the 21st century is to prevent the need for liver transplantation in as many patients with cirrhosis as possible.

Conflicts of interest

We declare that we have no conflicts of interest.

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