60. THE CLINICAL COURSE OF CIRRHOSIS

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Introduction. Cirrhosis represents the culmination of decades of liver injury and is thought to represent an irreversible disease. The clinical course of cirrhosis includes several disease states which require multistate models and competing risks analysis for proper assessment. Clinical states are defined according to the type of decompensation and increasing mortality. The traditional multistate models of cirrhosis have been validated in several studies and are currently widely used in clinical practice but mainly focus on the natural history of patients that are relatively stable.

Aim of study. Liver cirrhosis is characterized by a silent phase until decompensation, which is defined by ascites, bleeding from esophageal varices or hepatic encephalopathy. Herein, we aimed to analyze and characterize the clinical course and survival in cirrhosis.

Methods and materials. An advanced search was performed in the PubMed, Medline, and ScienceDirect databases, taking into account relevant articles, published in the last 10 years. The search English terms used were: ”Cirrhosis”,”Portal hypertension”,”Clinical states”,” Multistate model”,”Prognosis”

Results. Cirrhosis is classified as compensated or decompensated, based on the absence or presence of complication such as variceal bleeding, ascites, jaundice or encephalopathy. More recently, it has been recognized that increasing portal hypertension and several major clinical events are followed by a marked worsening in prognosis, and disease states have been proposed accordingly in a multistate model. The clinical course of cirrhosis may not be considered as unidirectional anymore . Aetiological treatment of cirrhosis may halt or even reverse the clinical course of the disease, particularly when it is still in a compensated state. Therefore, watchful follow-up of patients in whom the cause of cirrhosis has been successfully treated is recommended. Several clinical conditions associated with significantly different outcomes have been proposed as relevant clinical states during the course of the disease. Clinical states of cirrhosis are based on distinct outcome patterns and have a prognostic classification value. The progression of cirrhosis across clinical states is not predictable, although it parallels the progression of liver damage with its haemodynamic, inflammatory and functional consequences. However, it is notable that there is no predictable sequence of such clinical states and that they may not be considered as progressive disease stages. However, clinical states enable the classification of patients according to increasing mortality risk. Moreover, assessing transitions across states may facilitate the description of the clinical course of the disease in a multistate model. Compensated cirrhosis without varices (state 1). This is the earliest clinical state with a low incidence rate of decompensation and very low mortality. Compensated cirrhosis with varices (state 2). These patients are at risk of variceal bleeding and decompensation. Thus, they require a different monitoring schedule and specific treatment according to the severity of risk. Variceal bleeding (state 3). Patients with bleeding alone have better outcomes than patients with ascites without bleeding, and much better outcomes than patients with bleeding and ascites. First non-bleeding decompensation (state 4). Ascites is the most frequent first non-bleeding decompensating event and is in fact considered the hallmark of decompensation. Further decompensation (state 5). Following any first decompensating event, most patients develop further decompensation before dying. The most frequent combination is bleeding and ascites, although jaundice and encephalopathy are also frequent. Late advanced decompensation (state 6). The progressive increase in splanchnic vasodilatation, hyperdynamic circulation, bacterial translocation and systemic inflammation result in a more advanced, late decompensation state where multi-organ dysfunction becomes clinically evident.

Conclusion. The development of multistate models implies the assessment of the probabilities of more than one possible outcome from each disease state. Recognising different clinical states of cirrhosis may have important implications on the most likely clinical outcomes. Hence, clinical states may be used to inform treatment interventions to prevent disease progression.