The Consequences of Cirrhosis in America

Syed-Mohammed R. Jafri · Stuart C. Gordon

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In the evolution of liver disease, the phase between the development of cirrhosis and the development of complications, termed decompensated cirrhosis, is often prolonged, with a reported median survival of 12 years [1]. The development of cirrhotic complications (variceal bleeding, overt encephalopathy, infection, cancer, renal failure, ascites and hepatic hydrothorax) has immediate implications as it relates to the utilization of health care; moreover, such complications herald the larger risk of future clinical deterioration [2]. Development of any one of these complications denotes a turning point in the life of the cirrhotic patient. Hospitalization for a decompensation event markedly changes the median survival of the cirrhotic patient to <2 years [3]. Quality-of-life and mobility decline followed by a progressive rise of healthcare expenditures.

Individuals with compensated and decompensated cirrhosis have significantly worse health status, have more comorbid conditions and have a greater use of healthcare services including hospital visits, nursing homestays and physician visits compared to an age-matched patients without cirrhosis [4]. Rakowski et al. [4] reported the profound functional disability in cirrhotics as it relates to activities of daily living. Cirrhotics receive double the informal caregiving hours compared with age-matched non-cirrhotics leading to monetary loss due to medications, medical fees, home health costs and missed wages by patients and relations. Bajaj et al. [5] observed that hepatic encephalopathy is associated with a significant decline in employment status and financial status and significant

increase in caregiver burden which rose with Model End-Stage Liver Disease score.

The prevalence of cirrhosis in the USA is expected to increase, attributed largely to an aging hepatitis C birth cohort and the rising incidence of nonalcoholic steatohepatitis [6]. In the face of heightened Medicare utilization by the baby boomers, the direct cost of managing chronic liver disease—even excluding hepatitis C therapy—exceeds US \$1.4 billion annually [7]. The clinical hepatologist, in turn, strives toward minimizing the emergency room visits, prolonged hospitalizations and costly therapeutic interventions that characterize this complex patient population.

In this issue of *Digestive Diseases and Sciences*, Otgonsuren et al. [8] focus on how to better understand the economic and medical outcomes of Medicare patients who suffer from decompensated cirrhosis. This timely study highlights the impact of complications of chronic liver disease in the growing Medicare population. The findings include a high rate of death over 1 year after evidence of decompensation, with a 70 % overall death rate within 1 year following a decompensation event. Despite an improvement in mortality over the study period, the study additionally reflects a significant overall cost increase from 2005 to 2010, coinciding with an increase in the rates of spontaneous bacterial peritonitis and bleeding esophageal varices. Additionally, there was an 11 % increase in ICU stays, which represented a major driver of costs.

In an attempt to determine the highest relevant predictors of mortality, the authors identified older age, a higher comorbidity index and male gender as major influences. While these factors are not surprising, the authors interestingly identified hepatocellular carcinoma (HCC) as a major predictor of cost as well as mortality. This finding adds to a growing body of literature documenting that the incidence of HCC is growing at an alarming rate in the

S. R. Jafri · S. C. Gordon (✉)
Department of Gastroenterology and Hepatology, Henry Ford
Hospital, 2799 W. Grand Boulevard, Detroit, MI 48302, USA
e-mail: sgordon3@hfhs.org

USA, primarily related to HCC and nonalcoholic fatty liver disease.

Simultaneously with these liver cancer statistics come a number of reports from around the world showing that antiviral therapy lessens the risk of HCC arising from chronic HBV infection [9]. Indeed, such therapy has also lessened the overall incidence of HBV-related liver decompensation in the USA [10]. Similar findings demonstrate that successful hepatitis C antiviral therapy likewise lessens the risk of liver-related carcinoma and mortality [11].

Thus, the fundamental challenge to controlling Medicare-related liver disease cost lies in the effort to prevent future decompensation events. Treatment of the underlying disease appears to prevent worsening of liver fibrosis and forestalls decompensation. Marcellin et al. [12] reported that long-term HBV suppression actually reverses fibrosis. New antiviral therapies and the development of anti-fibrotic agents would potentially improve quality-of-life and reduce future disease burden and costs related to cirrhosis. A reduction in incidence and prevalence of cirrhosis, viral hepatitis and nonalcoholic liver disease would be projected to significantly reduce incidence of hepatocellular carcinoma and decompensation [13].

Fundamental to reducing the risk of cirrhosis-related complications includes the ability to effectively and inexpensively diagnose cirrhosis in asymptomatic subjects. Oftentimes the initial clinical manifestation of cirrhosis is evidence of complications in an undiagnosed, asymptomatic individual. Since cirrhosis evolves insidiously, without pain or symptoms, and since widespread screening for its most common etiologies (viral hepatitis and fatty liver) is not a routine practice, patients with compensated cirrhosis are often not aware that they have advanced liver disease. Clinical indices and features such as the lowering of the peripheral platelet count and serum albumin concentration and growing spleen size evolve over many years and often fall below the physician's threshold for further testing. The recent Food and Drug Administration approval of transient elastography should enable more widespread application of a noninvasive modality to establish this crucial diagnosis. Early diagnosis of cirrhosis, whatever its etiology, can facilitate appropriate intervention and thus reduce the probability of potentially lethal outcomes.

This change in practice, however, will require a substantial expenditure in current and near-future health care for birth cohort screening and disease-directed therapy for hepatitis C and nonalcoholic steatohepatitis. Measurement of disease burden with birth cohort-related screening and noninvasive evaluation of liver fibrosis would allow for identification of disease at an earlier stage. Cost of hepatitis

C management will be measured by cost/sustained virological response. This short-term cost will be significant, likely at an estimated \$100,000–\$150,000 per cure [14], substantially mitigated by the avoidance of higher longer-term costs of managing patients who, via the natural history of their disease, eventually develop complicated decompensated cirrhosis. Allocation of resources for this vulnerable population should justify the use of curative therapy to halt progression of liver disease before it reaches the precipice of decompensation.

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