Invited Editorials

process in hepatic venous outflow tract obstruction depends upon degree, site and length of obstruction, which may influence deterioration despite initial liver specific good scores.⁷

The editorial quoted that a report from Mumbai indicates that anticoagulation alone can achieve a complete clinical and laboratory response in 61% of patients followed up for a median of 21 months⁸. However, our interpretation of the study differs. Only 7/43 (16%) with anticoagulation had documented recanalization on imaging; whereas 9/11 (81.2%) who underwent radiological intervention had restoration of the outflow tract.

The success of the angiographic intervention was objectively documented by restoration of blood flow across the narrowed segment with its phasic respiratory variation. We agree that documentation of the disappearance of the pressure gradient across the obstructed segment would have objectivized the response more robustly. But our follow-up and associated clinical response albeit subjective was additional inputs for response.

As TIPSS results in the portal venous inflow bypassing the liver, it is not physiological in comparison to angioplasty. Long-term follow-up comparisons of hepatic venous outflow tract obstruction patients undergoing angioplasty/stenting and TIPSS were needed to establish whether a physiological approach should be first line of therapy in such patients and TIPSS should be offered with failure of such intervention. We also devised a sim-

ple prognostic score (AIIMS-HVOTO Score) which can identify patients for liver transplant in hepatic venous outflow tract obstruction patients.

ACKNOWLEDGEMENT

The authors' declarations of personal and financial interests are unchanged from those in the original article.²

REFERENCES

- Valla C, Payancé A. Editorial: short-length stenoses of hepatic venous outflow tract: an Asian specificity? *Aliment Pharmacol Ther* 2016; 44: 200–1.
- Shalimar, Kumar A, Kedia S, et al. Hepatic venous outflow tract obstruction: treatment outcomes and development of a new prognostic score. Aliment Pharmacol Ther 2016; 43: 1154– 67
- 3. Valla D, Hadengue A, el Younsi M, et al. Hepatic venous outflow block caused by short-length hepatic vein stenoses. *Hepatology* 1997; **25**: 814–9.
- Seijo S, Plessier A, Hoekstra J, et al. Good long-term outcome of Budd-Chiari syndrome with a step-wise management. Hepatology 2013; 57: 1962–8.
- Gracia-Pagan JC, Heydtmann M, Raffas S, et al. TIPSS for Budd-Chiari syndrome: longterm results & prognostic factors. Gastroenterology 2008; 135: 808–15.
- Pavri TM, herbst A, Reddy R, Fords KA. Budd-Chiari syndrome: a single center experience. World J Gastroenterol 2014; 20: 16236–44
- Paul SB, Shalimar Sreenivas V, Gamanagatti SR, Sharma H, Dhamija E, Acharya SK. Incidence and risk factors of hepatocellular carcinoma in patients with hepatic venous outflow tract obstruction. *Aliment Pharmacol Ther* 2015; 41: 961–71.
- 8. Shukla A, Bhatia SJ. Outcome of patients with primary hepatic venous obstruction treated with anticoagulants alone. *Indian J Gastroenterol* 2010; **29**: 8–11.

Editorial: the burden and aetiology of liver cirrhosis, and the risk of death

M. A. Konerman* & R. Loomba^{†,‡,§}

*Division of Gastroenterology and Hepatology, Department of Medicine, University of Michigan, Ann Arbor, MI, USA.

[†]NAFLD Research Center, University of California at San Diego, La Jolla, CA, USA.

[‡]Division of Gastroenterology, Department of Medicine, University of California at San Diego, La Jolla, CA, USA.

§Division of Epidemiology, Department of Family and Preventive Medicine, University of California at San Diego, La Jolla, CA. E-mail: roloomba@ucsd.edu

doi:10.1111/apt.13658

Assessing the burden of liver cirrhosis remains pertinent from a public health standpoint, as end stage liver disease is among the top 10 leading causes of death worldwide.^{1–3} Beyond attributable cause of death, liver cirrhosis is a chronic condition that can necessitate substantial medical care. As a result, cirrhosis accounts for significant health care costs with estimates upwards of \$2.5 billion per year in the USA alone.⁴ Although there have been many studies on the incidence, prevalence and natural history of liver cirrhosis, studies generated from the Swedish health care system offer specific advantages due to the nature of their single-provider, well-characterised public health care system.⁵

In a recent issue of *Âlimentary Pharmacology and Therapeutics*, Nilsson *et al.* characterised the overall burden of cirrhosis in southern Sweden from 2001 to 2011.⁶ Using the population-based medical registries in Sweden, the authors identified 1317 patients with cirrhosis. Patients were followed up for a median of 4.3 years and the annual incidence of liver cirrhosis was estimated as 14.1/100 000. Alcoholic related liver disease was the

overwhelming aetiology (58%) and ascites was the primary clinical manifestation at the time of diagnosis (43%). The 1-, 5- and 10-year survival rates were found to be 79%, 47% and 27% respectively. Furthermore, men and patients with HCV with concomitant alcoholic liver disease had the worst survival rates.⁶

This study has several strengths including a large sample size, length of longitudinal follow-up and robust data available for review given the medical infrastructure in Sweden. There are a few notable limitations and unaddressed questions that remain however. Inherent to any retrospective study are the limitations in terms of accurately identifying patients with cirrhosis, capturing complications from cirrhosis, and relevant comorbidities.⁷ Assessing the presence of alcohol abuse is particularly difficult, and in this study is likely under-represented as it was defined using only presence of these diagnoses in the patient's medical chart. The author's approach to categorization of aetiology of liver disease is also of interest, specifically the reliability of the diagnosis of NASH and the separation of NASH and cryptogenic cirrhosis. It would have been of interest to also evaluate these two groups combined given that prior studies have demonstrated that significant proportions of patients defined as having cryptogenic cirrhosis were likely due to NAFLD.8 Last, it would be of interest to outline the rank in the order of aetiologies of cirrhosis on burden of death.

Overall this study adds to the existing body of literature on the global disease burden, natural history, and associated morbidity and mortality related to end stage liver disease. In particular, this study emphasises the importance of addressing modifiable risk factors, specifically alcohol overuse as this aetiology portended a worse prognosis in this cohort. In the wake of the impact of direct-acting anti-virals for chronic hepatitis C, alcohol related liver disease and non-alcoholic fatty liver disease will account for progressively larger proportions of the patient population with chronic liver disease and thus

represent target areas for research and clinical attention.⁹ Future studies are needed to identify means to improve outcomes among these high risk patient populations.

ACKNOWLEDGEMENTS

Declaration of personal interests: None.

Declaration of funding interests: RL was supported in part by the American Gastroenterological Association (AGA) Foundation – Sucampo – ASP Designated Research Award in Geriatric Gastroenterology and by a T. Franklin Williams Scholarship Award; Funding provided by: Atlantic Philanthropies, Inc, the John A. Hartford Foundation, the Association of Specialty Professors, and the American Gastroenterological Association and grant K23-DK090303 and R01-DK106419. MK was supported by the National Institutes of Health T32DK062708 training grant.

REFERENCES

- Mokdad AA, Lopez AD, Shahraz S, et al. Liver cirrhosis mortality in 187 countries between 1980 and 2010: a systematic analysis. BMC Med 2014; 12: 145.
- Udompap P, Kim D, Kim WR. Current and future burden of chronic nonmalignant liver disease. Clin Gastroenterol Hepatol 2015; 13: 2031–41.
- 3. World Health Organization. The top 10 causes of death. www.who.int/mediacentre/factsheets/fs310/en/index4.html. (accessed February 4, 2016).
- 4. Neff GW, Duncan CW, Schiff ER. The current economic burden of cirrhosis. *Gastroenterol Hepatol* 2011; 7: 661–71.
- Blachier M, Leleu H, Peck-Radosavljevic M, Valla DC, Roudot-Thoraval F. The burden of liver disease in Europe: a review of available epidemiological data. *J Hepatol* 2013; 58: 593–608.
- Nilsson EAH, Sargenti K, Lindgren S, Prytz H. Incidence, clinical presentation and mortality of liver cirrhosis in southern Sweden: a 10-year population based study. *Aliment Pharmacol Ther* 2016; 43: 1330–39.
- 7. Weickert U, Buttmann A, Jakobs R, Schilling D, Eickhoff A, Riemann JF. Diagnosis of liver cirrhosis: a comparison of modified ultrasound and laparoscopy in 100 consecutive patients. *J Clin Gastroenterol* 2005; **39**: 529–32.
- Caldwell SH, Oelsner DH, Iezzoni JC, Hespenheide EE, Battle EH, Driscoll CJ. Cryptogenic cirrhosis: clinical characterization and risk factors for underlying disease. *Hepatology* 1999; 29: 664-9
- 9. Younossi ZM, Stepanova M, Afendy M, et al. Changes in the prevalence of the most common causes of chronic liver diseases in the United States from 1988 to 2008. Clin Gastroenterol Hepatol 2011; 9: 524–30 e1; quiz e60.