have a biologically plausible explanation for why these relationships would differ in women as compared with men. The issues of a possible responder bias also need to be evaluated.

Excess weight, particularly visceral, is known to produce a 'pro-inflammatory' state,[4] and this may be relevant, especially if one accepts that low grade inflammation is an aetiological factor in functional GI disease.[5] The authors are to be congratulated for examining this issue in a large dataset to highlight this association, but I would also encourage them to review their available wealth of data (on diet, exercise, menopausal status, etc.), to dissect out any further clues which may help inform further studies in this field.

Functional GI disorders cost individuals and societies greatly, and efforts to review lifestyle, dietary, environmental and behavioural triggers, or co-factors which may be amenable to population level management scientifically are to be encouraged.

ACKNOWLEDGEMENT

Declaration of personal and funding interests: None.

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Editorial: hepatocellular carcinoma – a rare complication of hepatic venous outflow tract obstruction

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doi:10.1111/apt.13198

Hepatic venous outflow tract obstruction (HVOTO) is a rare cause of liver disease that tends to present in young adults with manifestations of portal hypertension. Although >80% of western HVOTO patients have an identifiable thrombophilic risk factor, most eastern HVOTO patients have idiopathic HVOTO and are more likely to present with both vena cava and hepatic vein occlusion.[1] Due to its low incidence worldwide, accurate estimates of the incidence and risk factors for HCC development in HVOTO are not well described.[2, 3] In a recent issue, Paul *et al.* report on the incidence of HCC in 413 HVOTO patients managed at a single referral centre in India over a 25-year time period.[4] The observed annual rate of HCC of only 0.35% per year is markedly lower compared to other more common causes of chronic liver disease (Table 1).[5, 6] The authors reported that all of the patients with HCC had evidence of cirrhosis. In addition, vena cava occlusion and older subject age were more common in the patients with HCC compared to controls, but the small number of HCC cases precluded a multivariate analysis. Interestingly, serum AFP levels were increased in >80% at the time of HCC diagnosis as noted in prior studies.[3]

Important inferences from this study include the much lower annual incidence of HCC in this large cohort of HVOTO patients (0.35%) compared to prior estimates (2–50%) reported in a recent meta-analysis.[7] Limitations of this retrospective case–control study include the lack of data on other established risk factors for HCC (i.e. anti-HBc status, smoking, alcohol consumption) and the potential for underreporting with only 17% of patients followed up for 5 years. Furthermore, establishing a diagnosis of HCC using contrast enhanced cross-sectional imaging criteria is particularly challenging in HVOTO patients due to their tendency to form arterialised liver nodules. The association between more extensive vena cava involvement with an apparent increased risk of HCC has been suggested in prior reports.[7] However, whether these vascular occlusion patterns simply increase the risk of HCC via accelerated fibrosis progression or through other mechanisms remain unclear.

In summary, HVOTO patients with cirrhosis appear to be at increased risk of developing HCC. Serum AFP testing may prove particularly useful for HCC surveillance in 'high risk' HVOTO patients as has recently been

Table 1 | Incidence and features of HCC in patients with chronic liver disease

	Hepatitis C	HBV	NASH	HVOTO	Congenital heart disease
Annual incidence	3–5% (cirrhotic)	3–8% (cirrhotic)	1–2%	0.35%	<1%
Established risk factors	Cirrhosis and advanced fibrosis Age, male gender	Cirrhosis and advanced fibrosis Age, infection duration Prolonged high HBV DNA/eAg+	Cirrhosis and advanced fibrosis	Cirrhosis	Cirrhosis
AFP utility in screening	Low Sensitivity Low PPV + false positives	Low Sensitivity Low PPV	Low sensitivity Low PPV	Sensitive and specific	Sensitive and specific
Worldwide disease burden	High (increasing)	High (stable)	High (increasing)	Very low (stable)	Low (increasing)

HCV, hepatitis C virus; HBV, hepatitis B virus; NASH, non-alcoholic steatohepatitis; HVOTO, hepatic venous outflow tract obstruction; AFP, alfa fetoprotein; PPV, positive predictive value.

reported in subjects with fibrotic congestive hepatopathy.[5] Additional prospective studies are now needed to determine if simple clinical parameters such as duration and type of HVOTO, subject age, and non-invasive estimates of fibrosis severity (i.e. magnetic resonance elastography) can further help identify 'high risk' HVOTO patients that may benefit from HCC surveillance.[8]

ACKNOWLEDGEMENTS

Declaration of personal and funding interests: Robert J. Fontana has been a speaker and consultant for the Chronic Liver Disease Foundation and has received research funding from Janssen, BMS, Gilead, and Vertex Pharmaceuticals.

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Editorial: hepatocellular carcinoma - a rare complication of hepatic venous outflow tract obstruction – authors' reply

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doi:10.1111/apt.13209

We thank Drs Parikh and Fontana for their comments regarding the results of our study.[1, 2] However, there are certain aspects, raised by Drs Parikh and Fontana that needs clarification.

We fully agree that the diagnosis of HCC in the background of HVOTO is extremely challenging and numerous benign-enhancing nodules can mimic HCC. However, we could confidently diagnose all 16 HVOTO –HCC patients by the EASL criteria.[3] All patients had associated features of cirrhosis on imaging. Liver masses depicted typical arterial enhancement with washout in