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Editorial: endoscopic inflammation in ileoanal pouches—does it really matter? Authors' reply

We thank Drs. Townsend and Subramanian for their interest in our study and appreciate their comments regarding endoscopic healing in pouch patients.[1,2] As noted in our discussion, we acknowledge the inherent limitations of our study including its retrospective nature, potential selection bias and lack of standardised endoscopic surveillance protocol. However, we think the results of our study still provide a novel observation regarding the prognostic importance of endoscopic activity in asymptomatic pouch patients. We think that acute pouchitis is a meaningful clinical outcome that impacts patients' quality of life with increasing evidence that some interventions (probiotics, dietary interventions) may decrease its occurrence. We agree that chronic pouchitis and pouch failure would be even more impactful outcomes; however, the overall number of patients with these events was low in our cohort. In addition, it is difficult to compare the relative performance of endoscopic findings with faecal calprotectin (FC) across studies, and such a comparison would require a study in which both endoscopic and FC data are available. We agree that prospective studies with protocolised pouch surveillance are needed to further define the importance (and attainability) of endoscopic healing in pouch patients.

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LINKED CONTENT

This article is linked to Kayal et al and Townsend and Subramanian papers. To view these articles, visit https://doi.org/10.1111/apt.15505 and https://doi.org/10.1111/apt.15536.

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Editorial: rapid disease progression in hepatitis delta—can we turn the tide?

Palom *et al* recently reported the results of a long-term follow-up study of patients with chronic hepatitis delta (HDV) enrolled from four academic hospitals in Spain.[1] Their findings illustrate some of the major challenges we face in the management of this deadly disease. First, patients with HDV typically present with low HBV DNA levels and with minimally elevated ALT, thus masquerading as inactive HBV carriers. A high index of suspicion is therefore required to prevent underdiagnosis.[2,3] This is especially important given the rapid disease progression of HBV-HDV co-infection. In the recent study, 30% of patients had cirrhosis at study entry, and 31% of

non-cirrhotic patients developed cirrhosis during follow-up. Sadly, these rates are similar to those reported in a cohort that enrolled patients from 1997 onwards.[4] Importantly, achievement of HDV RNA undetectability reduced the risk of progression to cirrhosis and improved survival, but did not reduce the risk of hepatocellular carcinoma (HCC). This is in line with studies of successfully treated patients with HBV or HCV cirrhosis, where HCC risk also remains considerable.[5,6]

At this time, (pegylated-)interferon ((PEG-)IFN) is the only treatment option for HDV. Treatment results in HDV RNA negativity in 30% of patients, but relapse rates are high and this cannot be prevented through adding tenofovir.[7,8] Response to (PEG-)IFN (defined as undetectable HDV RNA) has been shown to decrease the risk of liver-related morbidity.[9] In the current study, (PEG-)IFN was also associated with an improved prognosis, irrespective of HDV RNA response. Given the retrospective nature of this study, this finding should be interpreted with caution, as patients who received therapy may have had less advanced disease, and since inclusion of patients with a history of (PEG-)IFN therapy may have introduced bias. Finally, it appears that (PEG-)IFN therapy was not analysed as a time-varying covariate, which may also have influenced results. It therefore remains uncertain whether (PEG-)IFN treatment confers survival benefits in non-responders.

Given the low success rates with currently available therapies, identification of patients at highest risk for adverse outcomes remains important for patient management and counselling. In this study, a previously described baseline-event-anticipation (BEA) score was applied to predict outcomes during follow-up. There was a clear relationship between higher BEA scores and risk of liver-related events, with 80% of patients in the highest risk group experiencing an unfavourable outcome. However, only 6% of patients were identified as being at high risk. Risk mitigation strategies aimed at this subgroup would only reach a minority of patients with a future clinical event and would therefore have limited impact on overall survival in the HDV population.

In conclusion, the study by Palom *et al* paints a sobering picture of the state of the art of HDV management: diagnoses are frequently made when cirrhosis is already present, identifying patients at highest risk for adverse outcome remains challenging, and current therapies have limited response rates. Novel treatment options that can also be used in patients with advanced liver disease are therefore urgently needed.

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