optimal for assessing HE, suggesting this is routine is a spurious claim. In fact, few studies report NPT unless explicitly studying HE. Ironically, only a minority of patients in the surgical study quoted underwent NPT. In our study, HE was assessed by three experienced hepatologists.

The second relates to maturity of follow-up. We agree and acknowledge in the manuscript our intent to report long-term outcomes, especially related to future risk of minimal HE, cardiomyopathy, HCC, and TIPS patency.

Before addressing the controversial issue of MRB in adults, contextualizing the pediatric experience is warranted. MRB is performed by a select few with requisite expertise, carries significant morbidity (hemorrhage, re-operation, shunt thrombosis), fails in 20%, and as such is often salvaged by spleno-renal shunts (ironically sometimes exacerbating HE). This is not a benign operation. Interestingly, MRB was found to be no better than porto-systemic shunts in a recent meta-analysis of 257 children (Yamoto et al. 2021).[2] Nevertheless, this is where the clear role of MRB ceases. In our cohort, more than 70% exhibited splenic/superior mesenteric vein thrombosis, explicit contraindications to MRB by the authors' own references. Large cavernomas represent a significant intraoperative hemorrhage risk even in the most skilled hands. Portal vein plasticity and tolerance to augmented flow in middle-aged adults after years of scarring is limited.

Finally, the authors do not appear to fully understand the vascular anatomy in noncirrhotic adults with cavernoma. PVR-TIPS decompresses the cranial segment of the portal circulation, enhances splenic venous outflow, and relieves portal hypertension. The caudal segment is often unchanged, with mesenteric drainage persisting through a less pressurized cavernoma. The presence of cavernoma at baseline is why patients do not present with HE, and the persistence of a less pressurized cavernoma draining the mesentery following PVR-TIPS explains the lack of HE.

There is insufficient evidence to routinely adopt MRB in adults. The referenced 14-patient study spanning 21 years only further affirms the need for center expertise. Rather than dismissing PVR-TIPS, we would proffer a contrarian approach. Given their world-class on-site IR expertise, we recommend adding PVR-TIPS to their therapeutic arsenal in age/size appropriate candidates, rather than a "MRB for all" approach. As the adage goes, just as kids aren't small adults, adults aren't just big kids.

## CONFLICT OF INTEREST

Dr. Boike consults for and received grants from W.L. Gore and Associates Inc.

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# Letter to the editor: Liver transplantation following severe acute respiratory syndrome-coronavirus-2 vaccination–induced liver failure

To the editor,

Several case reports have described development of liver injury following severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) vaccination in HEPATOLOGY.[1,2] These cases showed autoimmune hepatitis (AIH) features, and all cases responded well to

corticosteroid therapy. Herein, we present a patient who underwent liver transplantation due to fulminant liver failure following vaccination with the BioNTech vaccine.

A 53-year-old previously healthy man received a first dose of BioNTech vaccine on the June 5, 2021. Ten days after vaccination, he developed mild abdominal pain, erythematous skin eruption, and pruritus. Initial laboratory findings were alanine aminotransferase (ALT) 333 (upper limit of normal [ULN] 55 U/L), aspartate aminotransferase (AST) 168 (ULN 34 U/L), alkaline phosphatase 102 (ULN 150 U/L), and total bilirubin 0.8 (ULN 1.2 mg/dl). The patient's symptoms were considered to be a hypersensitivity reaction. Oral antihistaminic therapy and topical steroids did not lead to clinical improvement. On day 18 after vaccination, prednisolone 32 mg/day for 10 days followed by 16 mg/day for 20 days was commenced. One week into the steroid course, symptoms significantly improved, and aminotransferases decreased (Figure 1).

The patient was reluctant to receive a second vaccine dose for fear of additional side effects but had travel plans and needed a full vaccination chart. He, therefore, scheduled a second Pfizer-BioNTech vaccine dose 6 weeks after the first dose. Following the second vaccination, similar symptoms reoccurred after a few days. The dose of prednisolone was increased to 32 mg/day, gradually tapered, and discontinued in mid-August 2021. One month after, he developed abdominal pain, myalgia, fatigue, and jaundice. The symptoms and laboratory findings did not improve over 10 days, and he was referred to a tertiary liver transplant center. At admission, ALT was 485, AST was 629, total bilirubin was 6.6 mg/dl, and the international normalized ratio was 1.36. Serum IgG levels were 28.3 (7.0–16.4 g/L). Viral serology was negative for hepatitis A–E, Epstein-Barr virus, cytomegalovirus, and herpes simplex virus. Antinuclear antibodies, smooth muscle actin, antimitochondrial antibodies, anti–liver–kidney microsome 1, liver cytosolic antigen 1, and anti–soluble liver antigen were all negative; and ceruloplasmin was normal.

The liver biopsy showed portal inflammation with interface activity and significant lobular necroinflammatory activity, hepatocellular rosette formation and emperipolesis that are typical components of AIH. Treatment with prednisolone (40 mg/day, i.v.) and plasma exchange did not improve the liver function. The patient developed HE and underwent living donor liver transplantation. One month after liver transplantation, he was alive with significantly improved laboratory findings.

We presented a report of severe outcome of liver injury that developed after SARS-CoV-2 vaccination. We are aware that it is difficult to establish a definitive causality between SARS-CoV-2 vaccine and hepatitis. However, our case demonstrates strong evidence of vaccine-induced immune-mediated liver injury. The patient developed liver injury after a first dose of Pfizer-BioNTech vaccine which on reexposure led to severe liver injury. Our case, along with other reports, suggests that AIH-like hepatitis may develop after

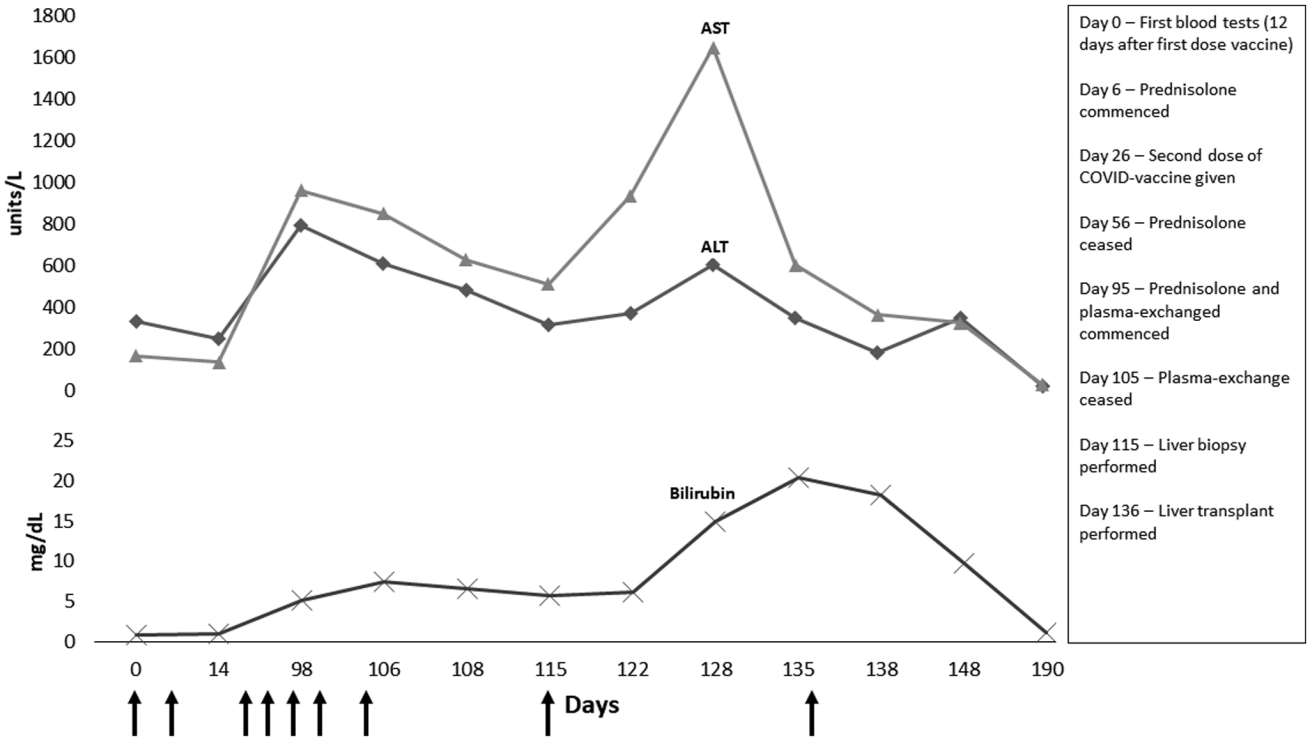


**FIGURE 1** Evolution of clinical and laboratory findings

SARS-CoV-2 vaccination. Early diagnosis and effective management seem to be very important in this emerging condition.

## CONFLICT OF INTEREST

Nothing to report.

## AUTHOR CONTRIBUTIONS

Cumali Efe, Murat Harputluoğlu, and Sezai Yilmaz conceptualized the study. Cumali Efe, Murat Harputluoğlu, and Neşe Karadağ Soylu collected and analyzed data. All authors approved the final version of the manuscript.

## DATA AVAILABILITY STATEMENT

All data that support the findings of this study are presented in the text.

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# Letter to the editor: Association between proton pump inhibitor use and biliary tract cancer risk: A Swedish population-based cohort study

To the editor,

With great enthusiasm, we read the article "Association Between Proton Pump Inhibitor Use and Biliary Tract Cancer Risk: A Swedish Population-Based Cohort Study" by Kamal et al.[1] It was propitious to read this manuscript, and the authors' endeavors are to be admired. We agree with the utmost conclusion that long-term utilization of proton pump inhibitors (PPIs) is significantly associated with biliary tree cancers. However, we deem it compulsory to state additional points that would augment the excellence of this article and add to former knowledge.

Firstly, historic cohort study design is of significant concern to the study's validity because of the risk of reporting bias and imprecise substantiation. For clarification, a 2006 study conducted by Cahan et al.[2] had a 1-month prospective follow-up that augmented their results. The authors were also able to elucidate interim PPI effects on the biliary tree along with long-term usage.[2] With great regard, the authors should also have explained the definite stature of gallbladder dysfunction due to this therapy. Likewise, gallbladder ejection fraction was one of the parameters in outlining the importance of preevaluation of gallbladder function before starting this medication.[2] By explaining the established diagnostic techniques, an accurate estimation of biliary tree functional status could be given. For this purpose,[2] hepatobiliary iminodiacetic acid scan, an effective diagnostic tool, is preferred in most cases. The authors have clearly explained the risks of infection due to long-term usage of PPI; however, they could not report a specific class of organisms involved in it. For instance, a 2014 study explained various tiny entities involved in oral flora, gastrointestinal tract, and environmental factors such as *Staphylococcus aureus*.[3] In addition, as they are entrenched, PPIs are involved in various changes in the body, such as PH and hormonal changes.[4] The authors should have described those changes associated with other significant gastrointestinal cancers. For representation,[4] different abdominal tumors, such as pancreatic cancers, biliary ductal cancer, ampulla cancer, and metastatic cancers, along with their specific locations, were explained, which will help find an association between PPI use and other accompanying cancers. As accepted, biliary tract obstruction is associated with worsening of the liver's physiology; authors should have delineated laboratory parameters