Reviewer #1:

1) Any evidence that cholangiocytes can support the replication of SARS-CoV-2? If any evidence, please mention in the text.
Answer: Due to the lack of suitable experimental models, tissue or organ tropism of the virus is not well established yet. The first autopsy with COVID-19 showed moderate microvesicular steatosis and mild lobular and portal activity, indicating the injury could have been caused by either SARS-CoV-2 infection or drug-induced liver injury. We have mentioned in the letter that ACE2 is significantly expressed just by cholangiocytes within the liver. Further research by Fudan University using human organoids showed that liver ductal organoids were susceptible to SARS-CoV-2 and viral replication was dramatic post-infection. SARS-CoV-2 infection induced cell death of host cholangiocytes and impaired bile acid transporting functions of cholangiocytes.

2) The authors should mention that vaccination also successfully eradicate poliovirus type 2 and 3, leaving wild type poliovirus 1.
We revise the manuscript according to the comment.

3) The authors should add briefly whether herd immunity is achievable through natural infection? So we need vaccination against COVID-19.
Answer: In Jun 2020, Kwok et cl calculated the threshold and the minimum proportion of total population required for herd immunity based on the number of new cases and the serial interval at that time. Given the mortality rate of 0.25–3.0%, herd immunity may be difficult to accept. However, the threshold might be changed according to the transmissibility of variants (more transmissible variant B.1.617.2) and the measures taken to control the virus. So, we won't know the actual threshold in real life, herd immunity can be observed with certainty only by analyzing the data in retrospect.

4) The authors mention, "mRNA COVID-19 vaccines are expected to have a favorable efficacy and safety profile in immunosuppressed patients and should be administered according to their standard dose and schedule. Liver transplant candidates with chronic liver disease should receive the mRNA COVID-19 vaccine prior to transplantation." Any evidence supporting this statement? How about protein subunit vaccine or other vaccine platform?
Answer: No large sample-size data is reported on COVID-19 vaccines inoculated in immunosuppressed patient. According to the efficacy and safety of other vaccines (Seasonal influenza vaccine, Adjuvanted subunit varicella zoster vaccine, etc.) using in solid organ transplant recipients, the immunogenicity of vaccines in recipients is lower than in immunocompetent individuals. So, it is recommended that vaccination should be completed prior to transplantation according to their standard dose and schedule. For patients with cancer, one dose of the BNT162b2 vaccine yielded poor

efficacy. Immunogenicity increased significantly in patients with solid cancer of a vaccine boost at day 21 after the first dose. Another novel study from Albert Einstein Cancer Center showed that comparing to solid tumors (98%), a significantly lower rate of seroconversion was observed in patients with hematological malignancies (85%), particularly recipients following highly immunosuppressive therapies such as anti-CD20 therapies (70%) and stem cell transplantation (73%). Patients receiving immune checkpoint inhibitor therapy (97%) or hormonal therapies (100%) demonstrated high seroconversion post-vaccination. Relatively lower immunogenicity was observed following vaccination with the adenoviral than mRNA-based vaccines.
Data is not sufficient to compare the efficacy of protein subunit vaccine or other vaccine platform using in liver cancer patients or candidates for liver transplantation.

5) I had some minor grammatical issue in the attached file.

Reviewer #2:

1) What about the safety of different types of COVID 19 vaccines in such group of patients espicillialy who are receiving immunosuppressive drugs?
Answer: No large sample-size data is reported on COVID-19 vaccines inoculated in immunosuppressed patient. According to the efficacy and safety of other vaccines (Seasonal influenza vaccine, Adjuvanted subunit varicella zoster vaccine, etc.) using in solid organ transplant recipients, the immunogenicity of vaccines in recipients is lower than in immunocompetent individuals. So, it is recommended that vaccination should be completed prior to transplantation according to their standard dose and schedule.

2) Not all countries espicially developping countries have mRNA vaccines...So,what about use of viral vector vaacines and some killed vaccines as sinopharm in that countries in such group of patients??
Answer: Study from Albert Einstein Cancer Center showed that comparing to solid tumors (98%), a significantly lower rate of seroconversion was observed in patients with hematological malignancies (85%), particularly recipients following highly immunosuppressive therapies such as anti-CD20 therapies (70%) and stem cell transplantation (73%). Patients receiving immune checkpoint inhibitor therapy (97%) or hormonal therapies (100%) demonstrated high seroconversion post-vaccination. Relatively lower immunogenicity was observed following vaccination with the adenoviral than mRNA-based vaccines.
Data is not sufficient to compare the efficacy of protein subunit vaccine or other vaccine platform using in liver cancer patients or candidates for liver transplantation.

It is a short letter to encourage CLD patients to receive COVID 19 Vaccines.. What about the safety of different types of COVID 19 vaccines in such group of patients espicillialy who are receiving immunosuppressive drugs? Not all countries espicially developping countries have mRNA vaccines...So,what about use of viral vector vaacines and some killed vaccines as sinopharm in that countries in such group of patients?? In the last paragraph, you reported that some people may still be infected with SARS COV2 after vaccination.However,they will be asymptomatic...I think ,many vaccinated people reinfected with COVID 19 but the symptoms were mild and did not require hospital admission.

Despite the large sample size in phase III trials, only few patients with mild to moderate liver disease (stable condition) were included and patients with immunosuppressive conditions were excluded. According to study from Albert Einstein Cancer Center, comparing to solid tumors (98%), a significantly lower rate of seroconversion was observed in patients with hematological malignancies (85%), particularly recipients following highly immunosuppressive therapies such as anti-CD20 therapies (70%) and stem cell transplantation (73%). Patients receiving immune checkpoint inhibitor therapy (97%) or hormonal therapies (100%) demonstrated high seroconversion post-vaccination. Relatively lower immunogenicity was observed following vaccination with the adenoviral than mRNA-based vaccines. For patients with cancer, one dose of the BNT162b2 vaccine yielded poor efficacy. Immunogenicity increased significantly in patients with solid cancer of a vaccine boost at day 21 after the first dose.

Both the viral vector vaccines, the inactivated vaccines and mRNA vaccines show efficacy against SARS-CoV-2 infection. But the safety of them is the major concern. Both AZD1222 and Ad26.COV2.S have been reported to be associated with thrombocytopenia and thrombus. Anvisa in Brazil said adenoviruses vaccine's potential dangers outweighed its benefits, and rejects used of adenoviruses vaccine. Furthermore, with the emergence of SARS-CoV-2 variants, the protective efficacy of different vaccines against variants vary greatly.