AASLD Nov. 12-15, 2021

The Liver Meeting®

DIGITAL **EXPERIENCE**

The Best of The Liver Meeting®

COVID-19 AND THE LIVER

About the program:

Best of The Liver Meeting 2021 was created by the Scientific Program Committee for the benefit of AASLD members, attendees of the annual conference, and other clinicians involved in the treatment of liver diseases. The program is intended to highlight some of the key oral and poster presentations from the meeting and to provide insights from the authors themselves regarding implications for patient care and ongoing research.

Use of these slides:

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Outcomes of post-vaccination COVID-19 after full or partial vaccination in patients with cirrhosis

Aim

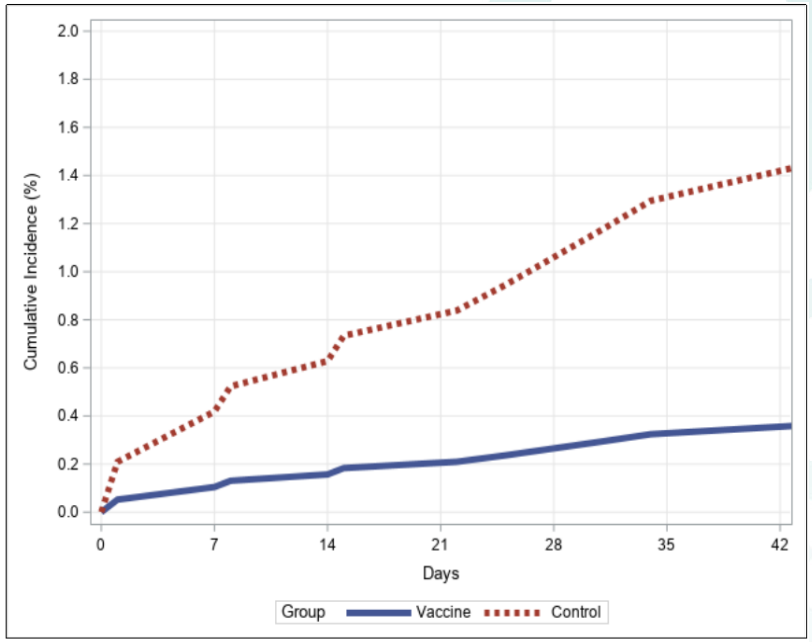
- To determine overall and COVID-related mortality in patients with cirrhosis and post-vaccination COVID-19

Methods

- Patients with cirrhosis and positive SARS CoV2 PCR between 3/1/2020 and 6/1/2021 included.
- Considered *fully vaccinated* if SARS CoV2 infection diagnosed 14 days after second dose of the Pfizer BNT162b2, Moderna mRNA 1273 mRNA vaccines, or single dose of the Janssen Ad.26.COV2.S vaccine.
- *Partially vaccinated* if SARS CoV2 infection diagnosed 7 days after first dose of any vaccine, but prior to full vaccination.

Main Findings

- In a multivariable analysis of a 1:2 propensity-matched cohort including vaccinated (n=254) and unvaccinated (n=508) participants, post-vaccination COVID-19 was associated with reduced risk of death (aHR 0.21, 95% CI 0.11-0.42)
- Reduction in mortality after both full (aHR 0.22, 95% CI 0.08-0.63) and partial vaccination (aHR 0.19, 95% CI 0.07-0.54)
- Following both 1273-mRNA (aHR 0.12, 95% CI 0.04-0.37) and BNT 162b2 vaccines (aHR 0.27, 95% CI 0.10-0.71)
- Among patients with compensated (aHR 0.19, 95% CI 0.08-0.45) and decompensated cirrhosis (aHR 0.27, 95% CI 0.08-0.90)



Estimated cumulative incidence rates of COVID-19 infection or death using multivariable Cox regression adjusted for age, BMI, race, tobacco use, and prior kidney transplantation; adjusted Hazard Ratio of Vaccine compared to control = 0.25, 95% CI 0.07-0.87, p=0.03

Conclusions

- Though patients with cirrhosis can develop breakthrough COVID-19 after full or partial vaccination, these infections are associated with reduced mortality.

John B, et al., Abstract 7.

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Early outcomes in liver transplant recipients during COVID-19 pandemic in the United States

Aim: To analyze the impact of COVID-19 pandemic on liver transplantation in United States

Methods: Comparison of patient characteristics and outcomes of liver transplantation during early COVID period (March 11-September 11, 2020) and pre-COVID period (March 11-September 11, 2019) using UNOS database.

Main Findings:

- Overall, 4% fewer liver transplantation were done during the COVID period (4107 vs. 4277).
- Alcoholic liver disease (32%) was the most common primary diagnosis during the COVID period with a significant increase (1315 vs 1187, p<0.01) from pre-COVID period.
- During the COVID period, liver transplant recipients had:
  - higher median MELD: (25 vs. 23, p<0.01)
  - lower time on the transplant wait list: (52 vs. 84 days, p<0.01)
  - higher need for hemodialysis before transplant: (457 vs. 404, p=0.01)
  - higher rate of multi-organ transplantation: (475 vs. 402, p=0.07).

Conclusions: During the COVID pandemic, overall rates of liver transplantation in US decreased, alcoholic liver disease was the primary diagnosis for liver transplantation, 90-day post-transplant graft survival was lower, and rate of organ rejection was higher.

Okumura K, et al., Abstract 13.

N		Pre COVID 4277	COVID 4107	p
Month, n(%)	Mar	747 (17.5)	572 (13.9)	<0.01
	Apr	703 (16.4)	606 (14.8)	
	May	676 (15.8)	768 (18.7)	
	Jun	686 (16.0)	678 (16.5))	
	Jul	673 (15.7)	723 (17.6)	
	Aug	792 (18.5)	760 (18.5)	
CIT, h median (IQR)		5.5 (4.4-7.0)	5.7 (4.7-7.0)	<0.01
Multi-organ, n (%)		402 (9.4)	435 (10.6)	0.07
<Induction>				
ATG, n (%)		320 (7.5)	189 (4.6)	<0.01
Basiliximab, n (%)		886 (20.7)	985 (24.0)	<0.01
steroids, n (%)		2363 (55.2)	2402 (58.5)	<0.01
Acute Rejection, n (%) (before discharge)		146(3.4)	185 (4.6)	0.02
LOS, days median (IQR)		10 (7-16)	10 (7-16)	0.5
90 day patient survival		96.6%	96%	<0.01
90 day graft survival		95.2%	94.5%	<0.01

CIT: cold ischemic time; ATG: anti-thymoglobulin; LOS: length of hospital stay

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COVID-19 vaccination is associated with reduced SARS CoV2 infection and death in liver transplant recipients

Aim

- Reports that post-transplant patients mount low anti-spike antibodies after COVID-19 vaccination have raised concerns. We studied the association between COVID-19 vaccination and COVID-19 infection or death in post-liver transplant patients.

Methods

- Liver transplant recipients from 12/15/2020 to 9/12/2021 were identified
- Patients considered fully vaccinated 14 days post second dose of either the Pfizer BNT162b2 mRNA or the Moderna 1273 mRNA vaccines.

Main Findings

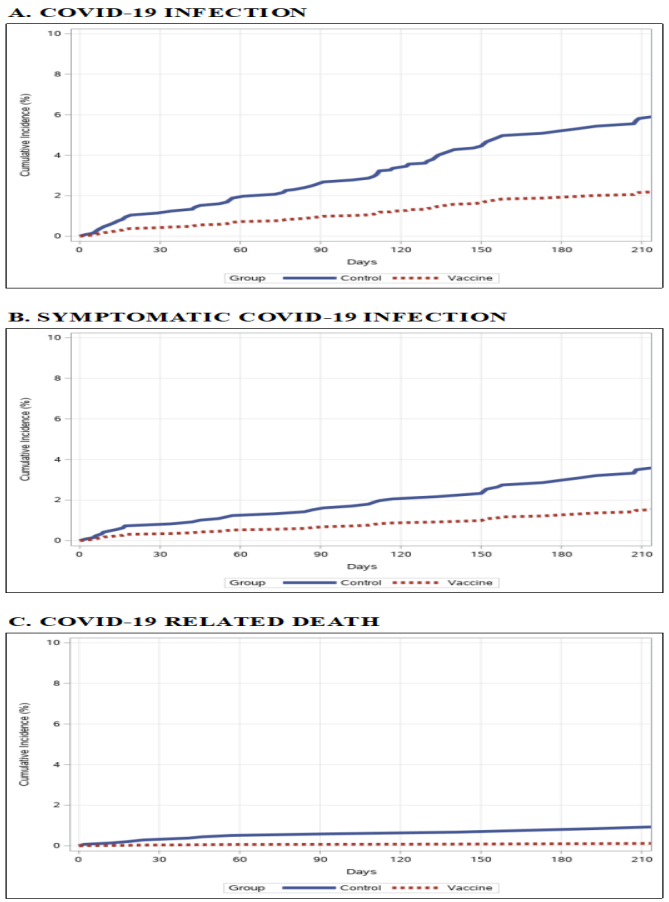
Full vaccination with a two-dose COVID-19 mRNA vaccine is associated with a

- 64% reduction in COVID-19 (aHR 0.36, 95% CI 0.26-0.51),
- 58% decrease in symptomatic COVID-19 (aHR 0.42, 95% CI 0.27-0.65), and
- 87% decrease in COVID-19 related death (aHR 0.13, 95% CI 0.04-0.37)

Conclusions

Two dose regimen of a COVID-19 mRNA vaccine is associated with a decrease in COVID-19 and death in liver transplant recipients. Findings suggest that vaccination may be more effective than suggested by antibody response.

John B, et al., Abstract 16.



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Association of BNT162b2 mRNA and mRNA-1273 vaccines with COVID-19 and hospitalization among patients with cirrhosis

Aim

- Cirrhosis is associated with immune dysregulation and vaccine hypo-responsiveness. This study aimed to investigate association of receipt of Pfizer BNT162b2 mRNA or Moderna 1273 mRNA vaccines and COVID-19, COVID-19 related hospitalization or death in patients with cirrhosis

Methods

- Retrospective cohort study of patients with cirrhosis who received at least one dose of a COVID-19 mRNA vaccine. Vaccinated Patients (n=20,037) were propensity matched with 20,037 controls to assess the associations of vaccination with COVID-19, hospitalization, and death.

Main Findings

- COVID-19 in vaccine recipients was similar to the control group in days 0-7, 7-14, 14-21, and 21-28 after the first dose.
- After 28 days, receipt of one dose of an mRNA vaccine associated with a 64.8% reduction in COVID-19 and 100% reduction in hospitalization or death due to COVID-19.
- Association of reduced COVID-19 was lower among patients with decompensated (50.3%) compared to compensated cirrhosis (66.8%).
- Receipt of a second dose associated with a 78.6% reduction in COVID-19 and 100% reduction in COVID-19 related hospitalization or death after 7 days.

Conclusions

- mRNA vaccine administration was associated with a delayed but modest reduction in COVID-19 but an excellent reduction in COVID-19 related hospitalization or death in patients with cirrhosis.

Table 2. COVID-19 Infection, Hospitalization for COVID-19, and COVID-19–Related Death After Administration of First Dose of the Pfizer BNT162b2 mRNA or the Moderna mRNA-1273 Vaccines

	Day 0-7		Day 7-14		Day 14-21		Day 21-28		Day 28-onward		Vaccine efficacy day 28 onward, % (95% CI)[a]	*P* value
Vaccine and control	Vaccine	Control	Vaccine	Control	Vaccine	Control	Vaccine	Control	Vaccine	Control		
COVID-19 infection												
No.	183										64.8 (10.9-86.1)	
Events, no.	25	36	21	32	17	12	14	8	6	17		
Cumulative events, no.	25	36	46	68	63	80	77	88	83	105		.03
No. at risk	20037	20037	18109	18073	15991	15935	13731	13678	12059	12012		
Cumulative incidence, %	0.12	0.18	0.25	0.38	0.39	0.50	0.56	0.64	0.69	0.87		
Hospitalization for COVID												
No.	57										100.0 (99.3-100.0)	
Events, no.	4	8	8	7	6	5	10	6	0	3		
Cumulative events, no.	4	8	12	15	18	20	28	26	28	29		.20
No. at risk	20037	20037	18109	18073	15991	15935	13731	13678	12059	12012		
Cumulative incidence, %	0.02	0.04	0.07	0.08	0.11	0.13	0.20	0.19	0.23	0.24		
COVID-19-related death												
No.	13										100.0 (99.3-100.0)	
Events, no.	1	3	2	1	0	2	1	1	0	2		
Cumulative events, no.	1	3	3	4	3	6	4	7	4	9		.20
No. at risk	20037	20037	18109	18073	15991	15935	13731	13678	12059	12012		
Cumulative incidence, %	0	0.01	0.02	0.02	0.02	0.04	0.03	0.05	0.03	0.07		

John B, et al., Abstract 38.

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Vaccination against COVID-19 decreases hospitalizations in patients with cirrhosis: results from a nationwide analysis

Objective

- To assess the impact of vaccination against COVID-19 in Chilean patients with cirrhosis

Methods

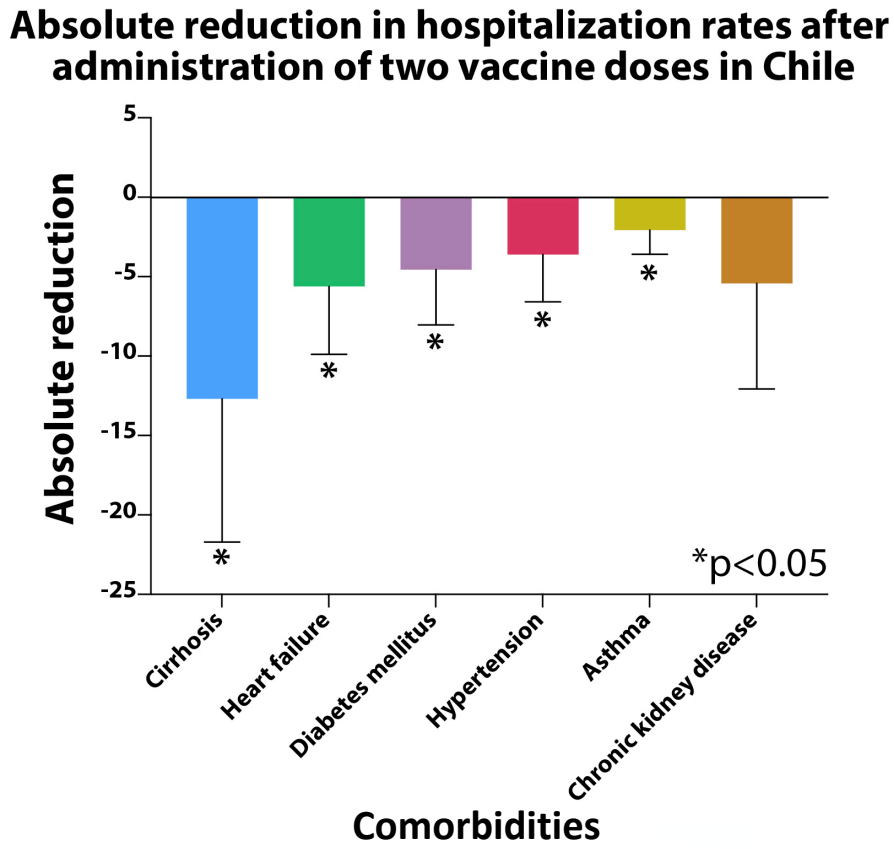
- Quasi-experimental design from nationwide data, using regression discontinuity models to estimate the hospitalization rates (recorded as a continuous variable beyond 14 days following the second vaccination dose)

Main Findings

- 1,648,680 COVID-19 cases. A total of 0.1% COVID-19 cases had underlying cirrhosis, and 42.9% required hospitalization.
- We observed a substantial decline of absolute hospitalization rates among patients with cirrhosis who were vaccinated versus those not vaccinated (-12.69, 95%CI -21.71 to -3.68; p <0.01).

Conclusions

- Our nationwide study showed an association between vaccination against COVID-19 and a lower hospitalization risk in patients with cirrhosis.



Diaz LA, et al., Abstract 39.

Limited TCR repertoire and aberrant CD39 regulation mark late-stage COVID-19

Objective

- Define gene signatures linked with immune alterations in COVID-19

Methods

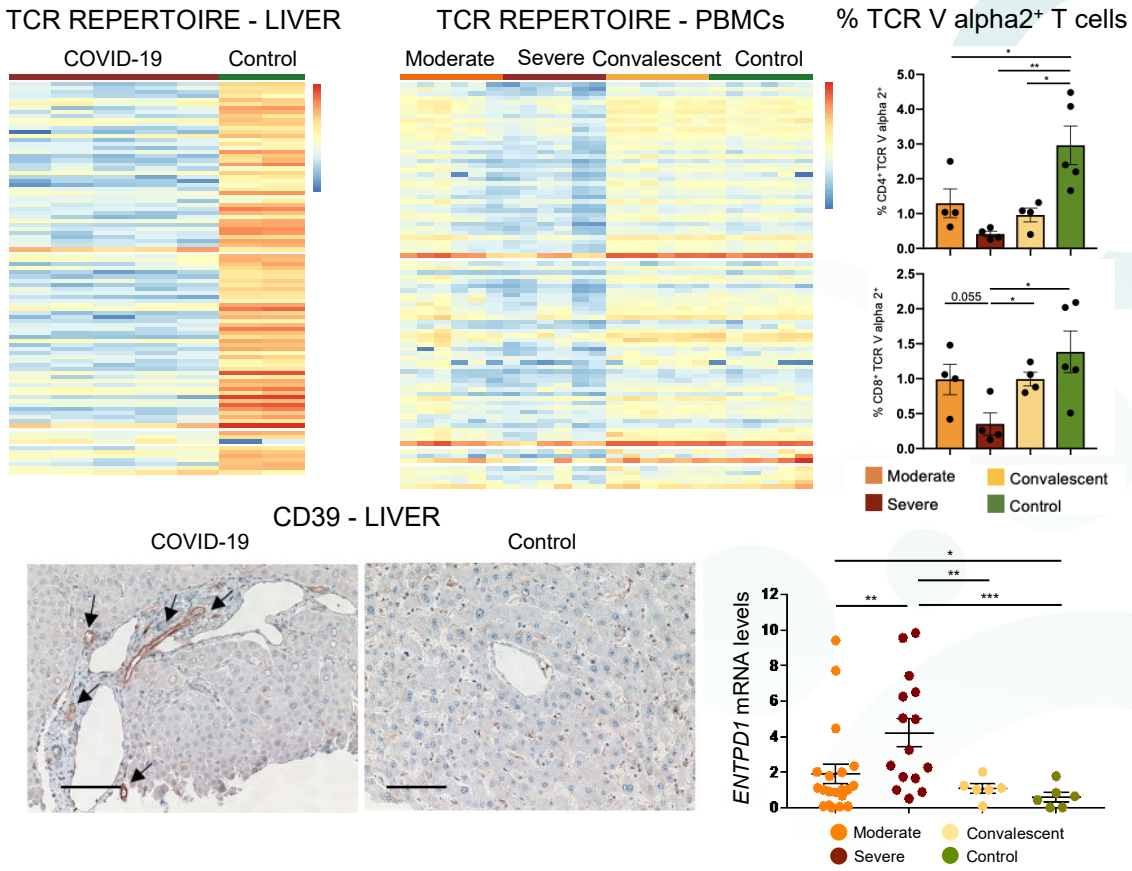
- Transcriptome analysis using NanoString Technologies of peripheral blood mononuclear cells (PBMCs) and ultrasound-guided biopsies from liver, lung, heart, kidney, and spleen
- COVID-19 patients (n=19 severe, n=21 moderate, n=10 convalescent); controls (n=12)

Main Findings

- Downregulation of TCR variable genes and increase in CD39 in the liver and PBMCs of severe COVID-19 patients

Conclusions

- Limited TCR repertoires and aberrant CD39 levels may contribute to immune imbalance in COVID-19. Interference with CD39 might prevent disease progression and stabilize patients with severe COVID-19



Longhi MS, et al., Abstract 68.

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Long-term clinical outcomes of patients with COVID-19 and chronic liver disease: US multicenter COLD study

Aim

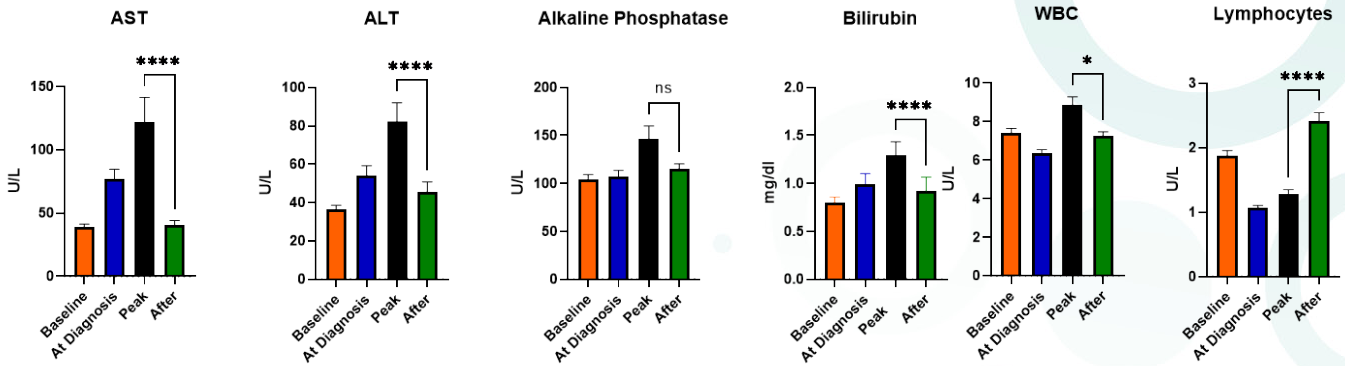
To understand the long-term consequences of coronavirus 2019 (COVID-19) in patients with chronic liver disease diseases (CLD)

Study Cohort

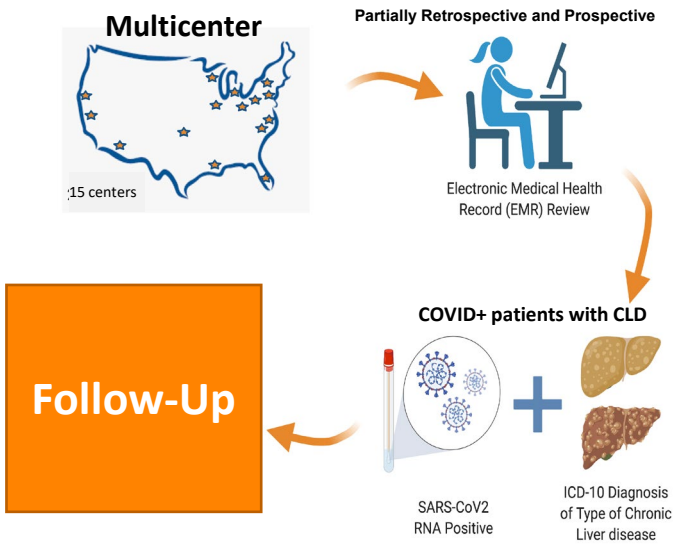
- 15 participating centers
- Median follow-up 364 days
- Total 321 patients

Lab Parameters

All the following lab parameters showed significant improvement after resolution of COVID-19.



Methods



Natural History

- Hospitalization rate during the follow up: 38.3% (n=123)
- Long COVID-19: 26.5% (n=85)
- Long-term mortality was 7.1% (n=23)

Sequelae

- Alcohol Use: 24.3% (n=78) patients reported moderate to heavy alcohol use
- Weight gain was noted in 32% (n=94) patients.

Vaccine Status: 70% had received COVID-19 vaccination

Implications

The acute liver injury and lymphopenia observed during COVID-19 resolved in most patients. However, we observed a high burden of morbidity with persistence of symptoms related to COVID-19, weight gain, and alcohol use.

Aby E, et al., Abstract 71.

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Delayed and suboptimal response to two doses of SARS-CoV-2 mRNA vaccine in European patients with compensated and decompensated cirrhosis of different aetiologies: interim analysis

Hypothesis and Aim

SARS-CoV-2 mRNA vaccines have been approved to prevent SARS-CoV-2 infection, with a reported efficacy of 95% in the general population, but response in patients with cirrhosis is still unknown.

Methods

- Prospective study to assess humoral and cellular response to vaccine in patients with cirrhosis compared to healthy controls according to previous SARS-CoV-2 infection.
- SARS-CoV-2 IgG antibodies directed against the Spike-protein and Nucleocapside (anti-S and anti-N Ab) were tested at baseline, **21 days after the first dose (V1)** and **21 after the second dose (V2)**.
- Healthy volunteers were tested at the same timepoints.
- In 13 unselected patients with cirrhosis, the cellular response to vaccine has been studied and compared to controls by quantification of IFN-g and IL-2 production.
- Side effects after vaccination were collected

Main Findings

- **182 patients with cirrhosis**

  age 61 years, 75% males, 59% viral-related cirrhosis, 74% Child-Pugh A, 31% HCC, 15% enlisted for liver-transplantation, 16% with a previous SARS-CoV-2 infection

- **38 healthy controls** (31% with a previous SARS-CoV-2 infection)

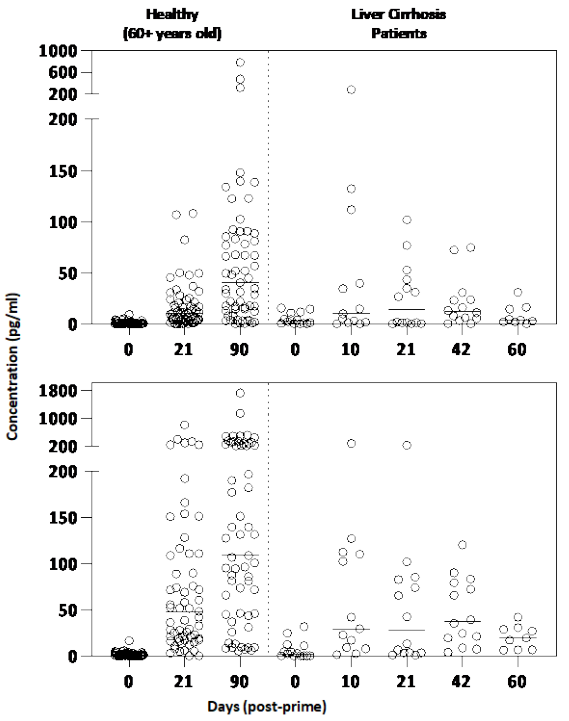
Conclusions

In patients with cirrhosis, specifically in those with advanced disease, response to SARS-CoV-2 vaccines was delayed and suboptimal compared to the general population

Humoral response to SARS-CoV-2 vaccination at V1 and V2 time-point in healthy controls and patients with cirrhosis stratified according to previous SARS-CoV-2 infection

	Cirrhosis (overall)	Controls (overall)	p	Cirrhosis with previous COVID-19	Controls with previous COVID-19	p	Cirrhosis w/out previous COVID-19	Controls w/out previous COVID-19	p
Anti-S V1, U/ml	22.8 (0.4-12,500)	84.75 (0.4-12,500)	0.0001	7,500 (0.4-12,500)	12,500 (8,952-12,500)	<0.0001	13.9 (0.4-12,500)	43.1 (0.4-345)	0.001
Anti S V2, U/ml	1,786 (0.4-12,500)	4,523 (259-12,500)	0.0004	7,500 (298-12,500)	12,500 (7,551-12,500)	<0.0001	1,034 (0.4-12,500)	1,520 (259-12,500)	0.05

Longitudinal evaluation of Spike T cell response in cirrhotics vs. healthy individuals



Humoral response to SARS-CoV-2 vaccination at V1 and V2 time-point in cirrhosis, w/out previous COVID-19, according to Child-Pugh

	Cirrhosis CPT A	Cirrhosis CPT B+C	p
Anti-S V1, U/ml	23.0 (0.4-12,500)	0.4 (0.4-109)	0.0003
Anti S V2, U/ml	1,377 (0.4-12,500)	637 (0.4-12,500)	0.01

Patients with HCC and undetectable anti-S Ab after V1 had significantly lower anti-S Ab titres after V2

Spike Gold stimulation
IFN-γ
IL-2

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Iavarone M, et al., Abstract LO11.

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