

What is challenging in the management of chronic liver diseases in 2020?

Lessons learned from COVID-19 in hepatology

Covid-19 and Liver Transplantation

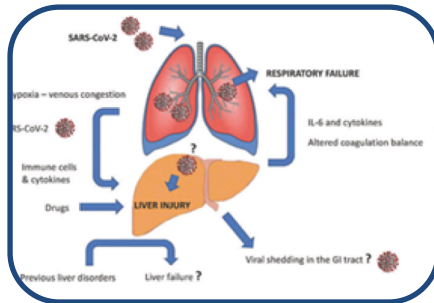


Disclosures

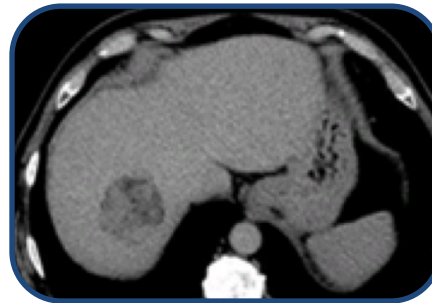
Marina Berenguer

- Abbvie: speaker, advisory board
- Gilead: Grant
- Novartis: speaker
- Astellas: speaker
- Intercept: advisory board. Speaker
- Orphan: advisory board
- Alexion: advisory board
- Deep genomics: advisory board

Agenda

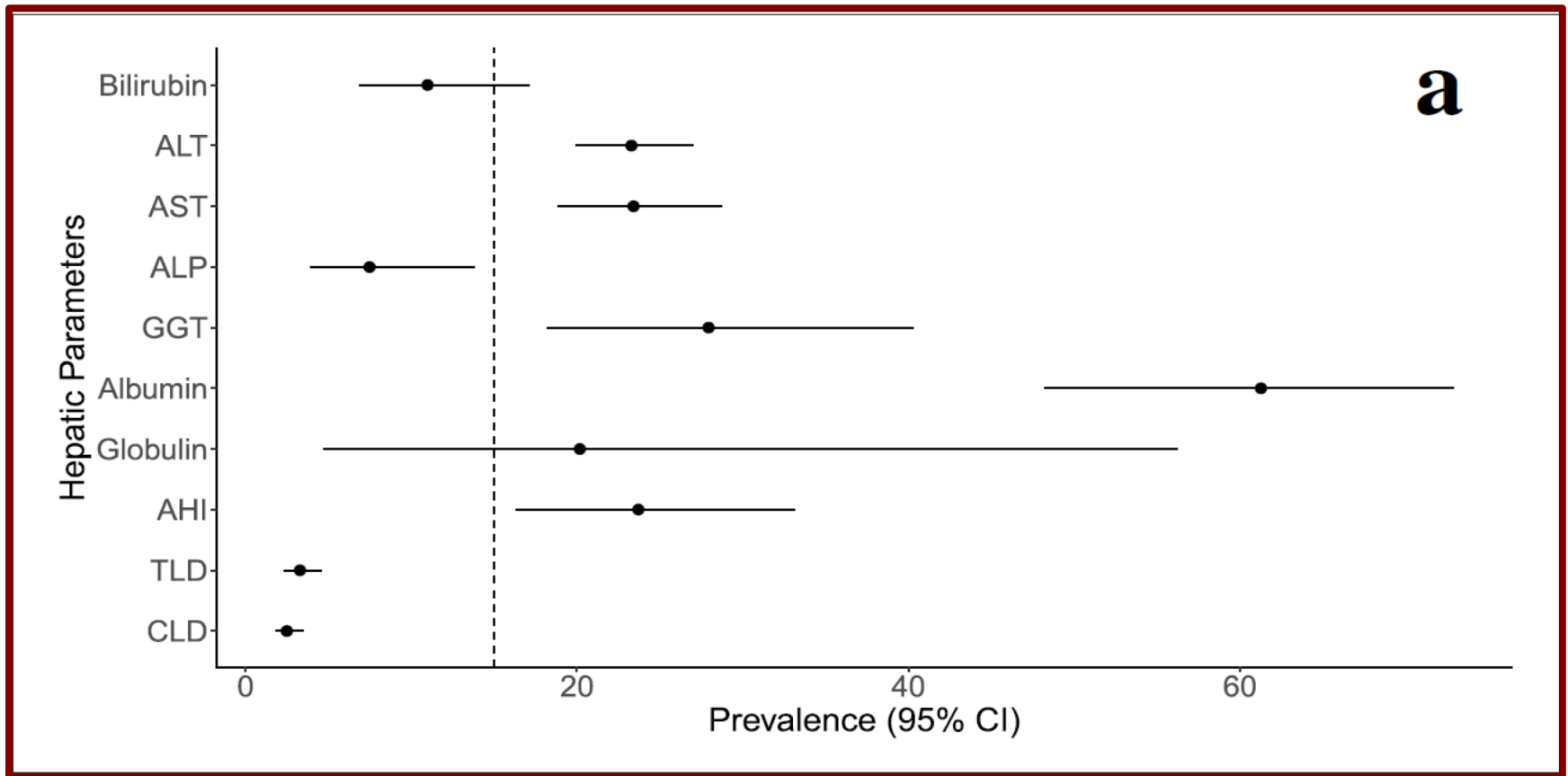


Covid and underlying
CLD (including HCC)



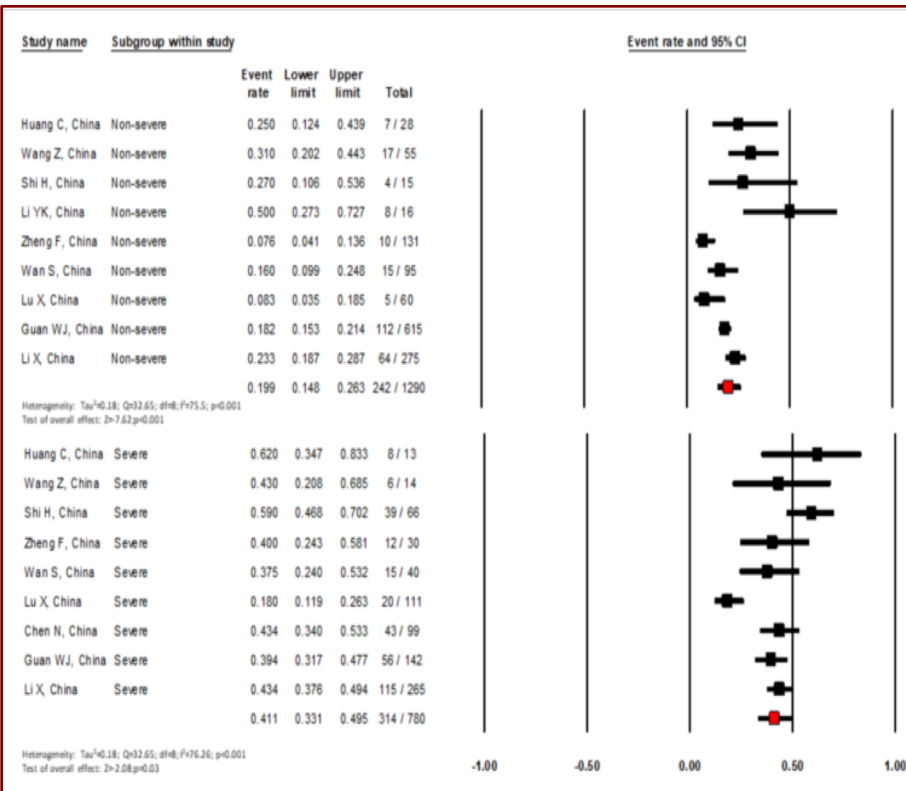
Covid and the LT
patient

Liver enzymes abnormalities

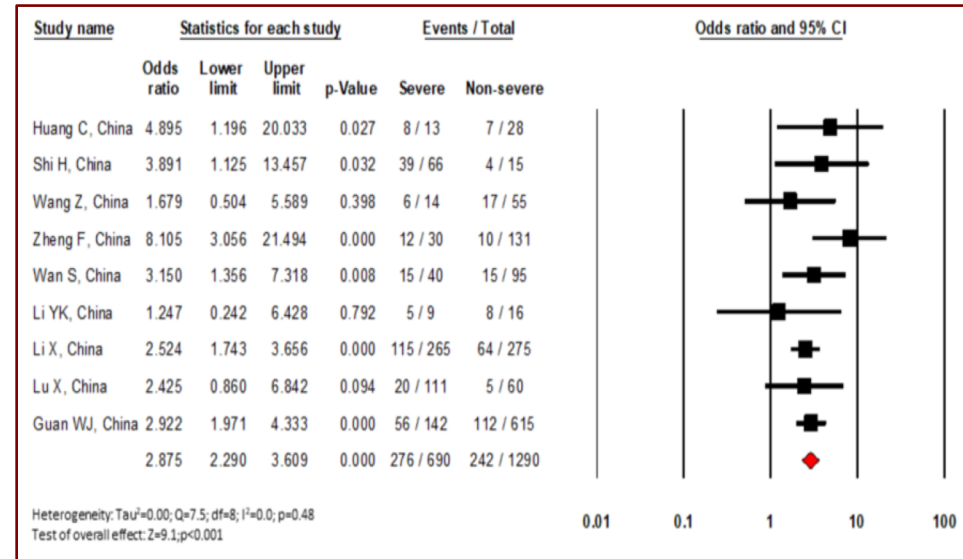


14%-53% of hospitalized patients (rate vary depending on geographic location, disease severity, timing of measurement, prevalence of underlying CLD...)

Liver injury and covid-19 disease severity



Forest plot of studies reporting the incidence of elevated liver chemistries in severely infected and non-severely COVID-19 patients

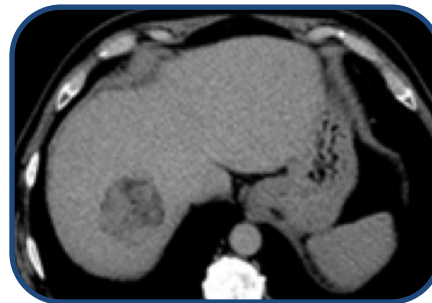
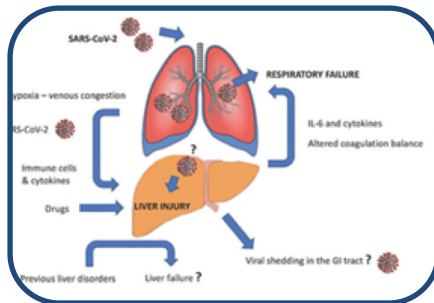


Forest plot showing the odds ratio of elevated liver chemistries at initial presentation in severe vs. non-severe COVID-19

Liver Injury is probably multifactorial



Agenda



**Covid and underlying
CLD (including HCC)**



Covid and the LT
patient

Chronic liver disease and covid 19

1) Rate of patients with CLD in covid-19 cohorts:

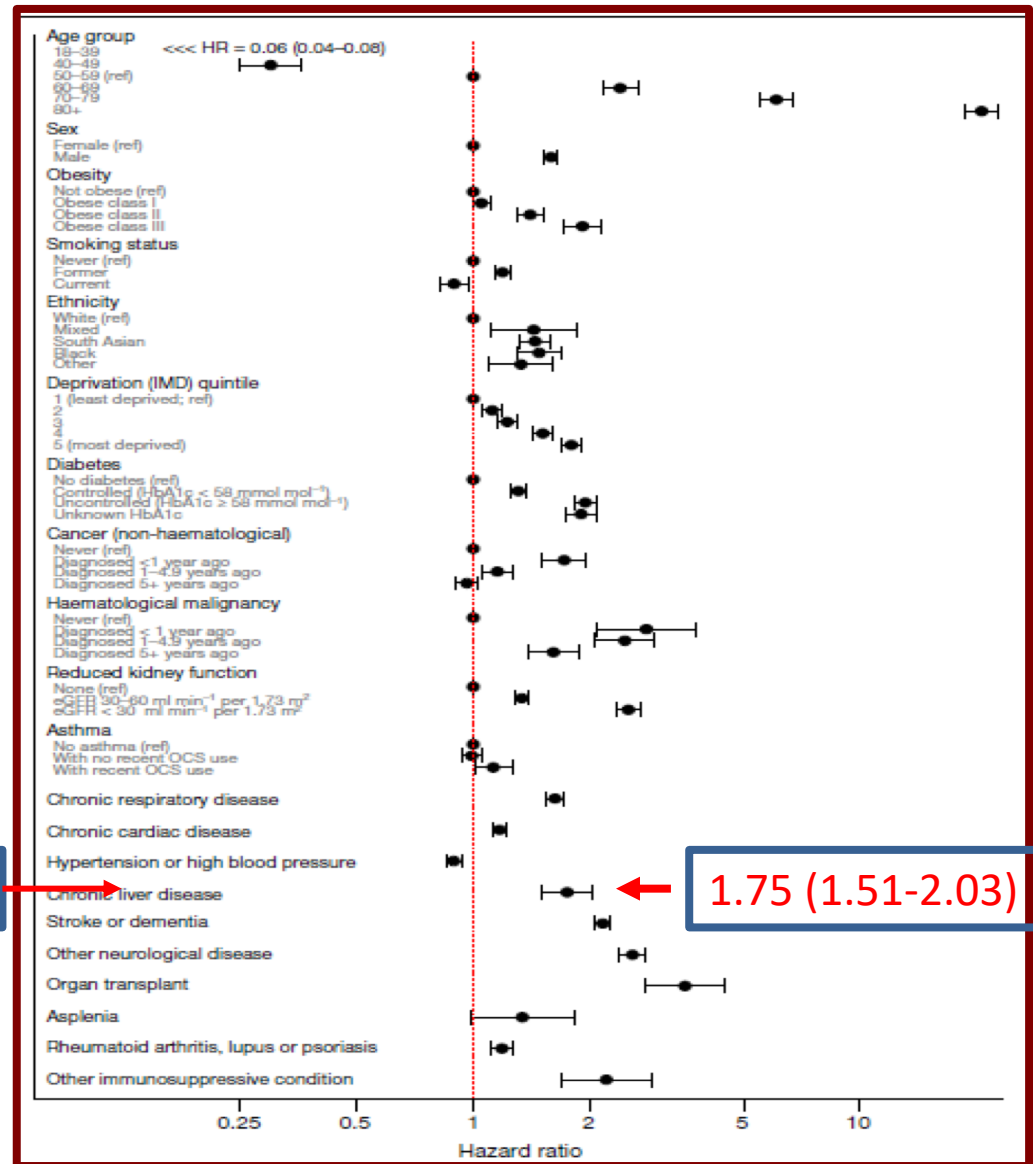
- 1-11%
- In the largest cohorts, less than 1%



CLD not over-represented in covid-19 cohorts

2- May be associated with worse outcome (increased hospitalization and death)

Chronic Liver Disease



17,278,392 adults pseudoanonymously linked to 10,926 covid-19 deaths

Chronic liver disease and outcome following covid 19 infection

	Before propensity matching			After propensity matching		
	COVID-19 with liver disease (n = 250)	COVID-19 without liver disease (n = 2530)	RR, RD, or <i>P</i> value	COVID-19 with liver disease (n = 250)	COVID-19 without liver disease (n = 250)	RR, RD, or <i>P</i> value
Outcomes						
Mortality, %, (n/total)	12.0 (30/250)	4.3 (110/2530)	RR: 2.8 (1.9, 4.0) RD: 7.7% (3.5%, 11.75%) <i>P</i> < .001	12.0 (30/250)	4.0 (10/250)	RR: 3.0 (1.5, 6.0) RD: 8.0% (3.3%, 12.7%) <i>P</i> = .001
Hospitalization rate	52.0 (130/250)	30.0 (760/2530)	RR: 1.7 (1.2, 2.0) RD: 22.0% (15.5%, 28.4%) <i>P</i> < .001	48.0 (120/250)	36.0 (90/250)	RR: 1.3 (1.1, 1.6) RD: 12.0% (3.4%, 20.6%) <i>P</i> = .006

2,780 covid-19 patients in the US
 150 (9%) with pre-existing liver disease (42% NAFLD)
 50 (1.8%) with cirrhosis

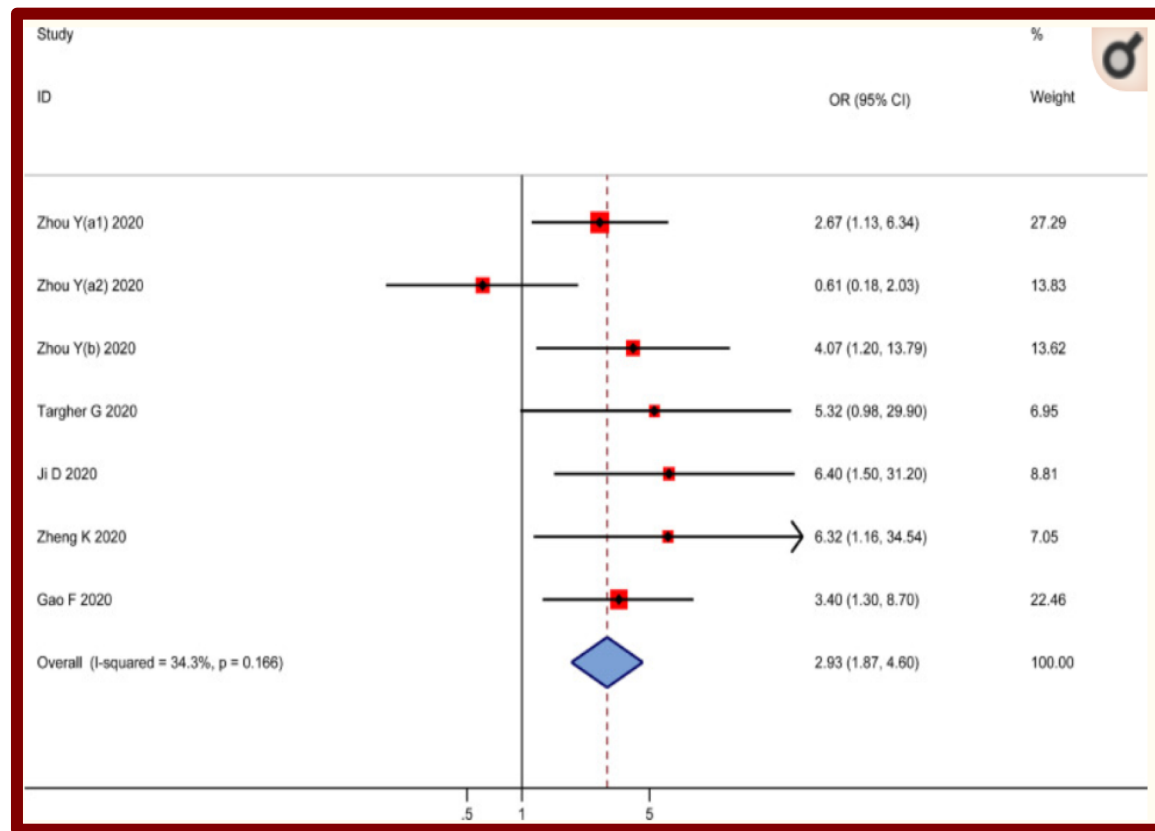
Metabolic associated fatty liver disease increases the severity of covid-19

* Covid-19 outcomes associated with DM, AHT, CVD, & obesity

* US steatosis & indirect markers of fatty liver:

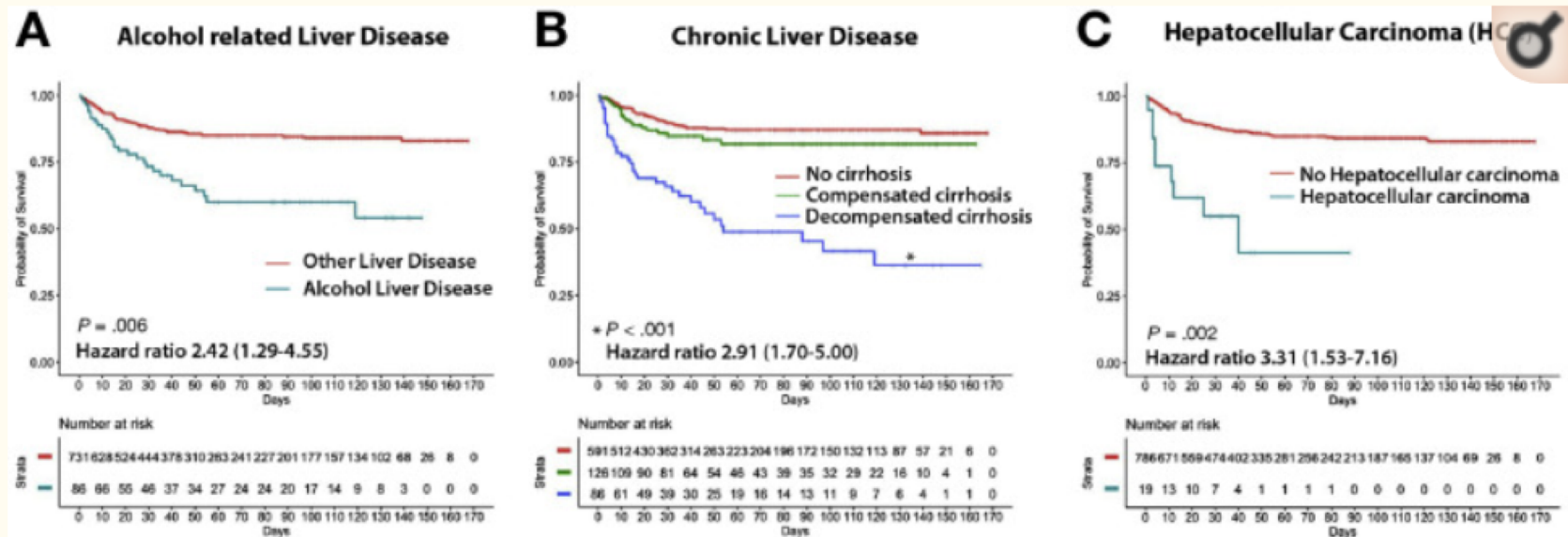
- Are common in cohorts with covid-19

- Have been associated with disease severity



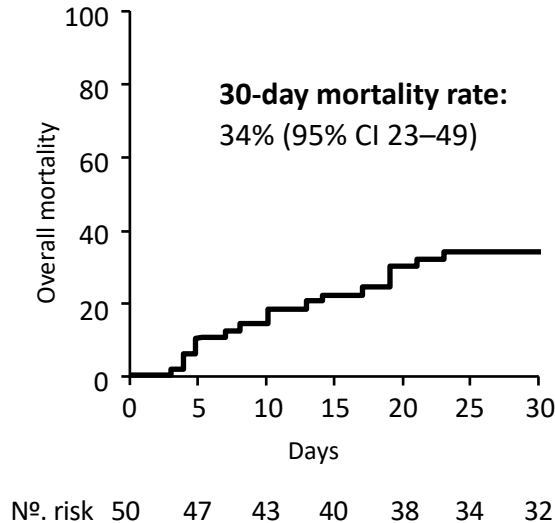
Other predictors of outcome in patients with underlying chronic liver disease

867 patients from 21 centers across the US with CLD with COVID-19



Is Severe Liver Disease or Cirrhosis Associated With Worse COVID-19 Outcomes?

Cumulative Probability of Overall Mortality



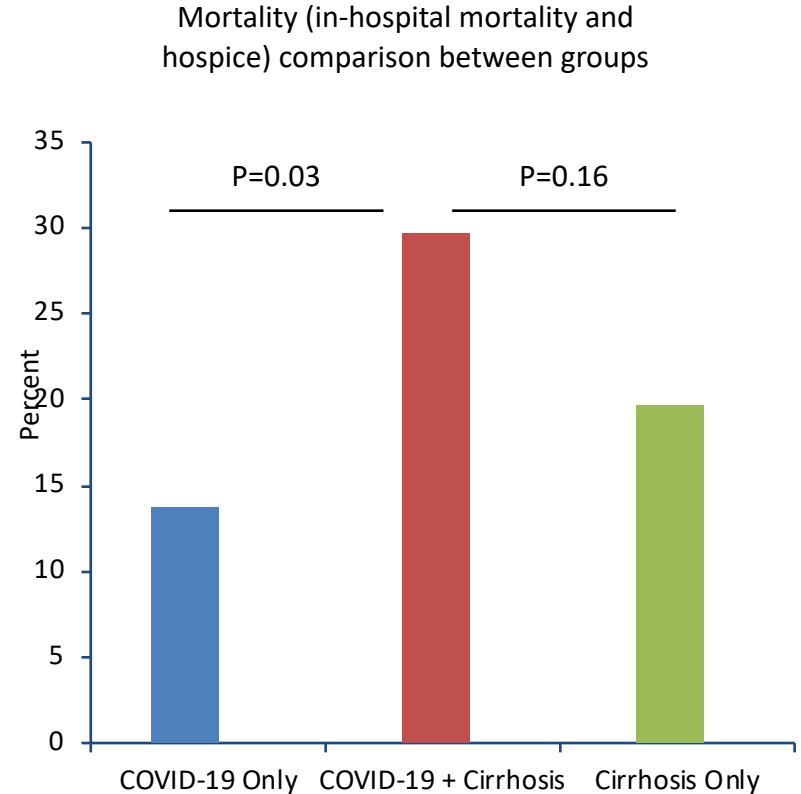
Cirrhotics with COVID-19 vs cirrhotics with bacterial infection:

34% (95% CI 23–49) vs 17% (95% CI 8–32), $P=0.03$

Cirrhotics with COVID-19 vs non-cirrhotics with COVID-19:

34% (95% CI 23–49) vs 18% (95% CI 15–22), $P=0.035$

Mortality comparison between groups



International
registry study

29 countries
130 centres
over 105 days

1365 patients included

745 chronic liver disease

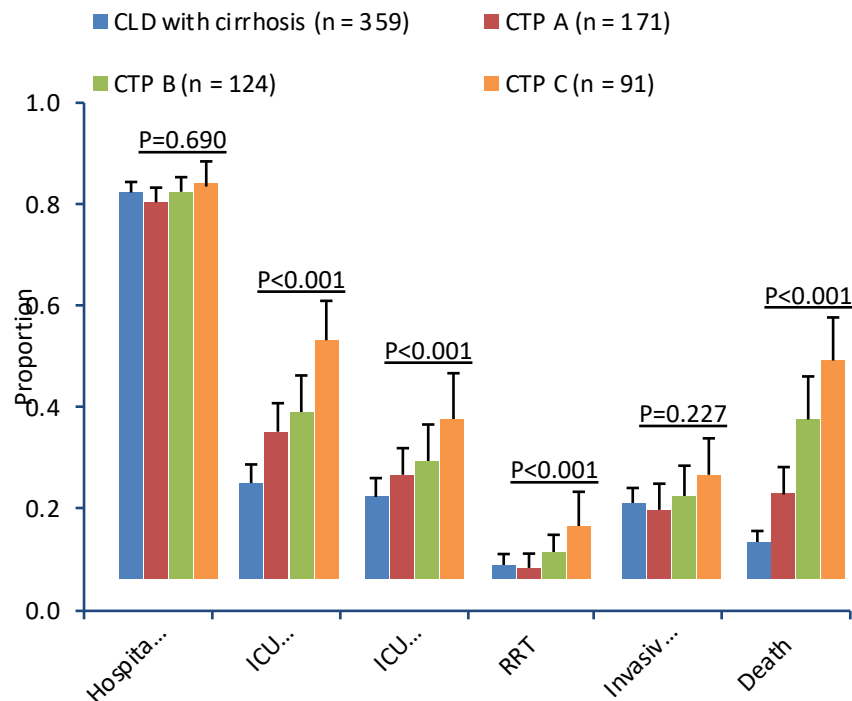
• 359 without cirrhosis

• 386 with cirrhosis

620 without liver disease

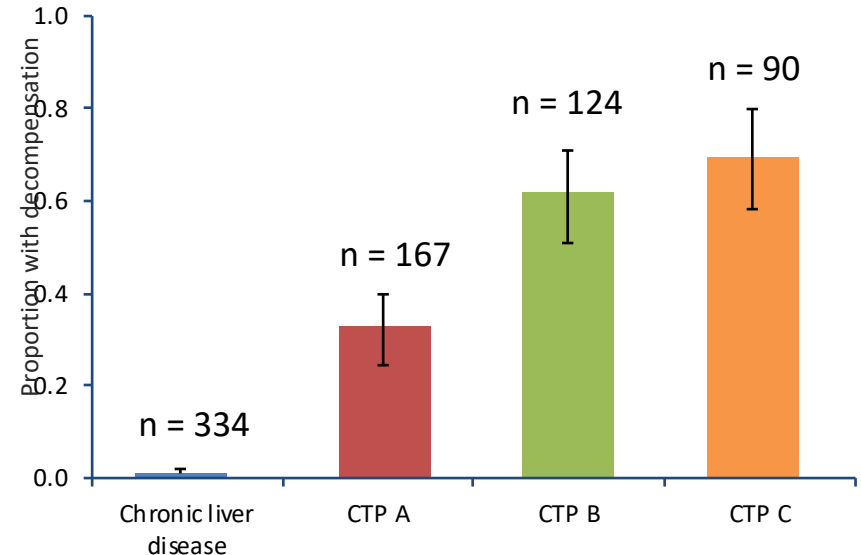
SARS-CoV-2 Infection in Patients with Chronic Liver Disease: Data From the COVID-Hep and SECURE-Cirrhosis Registries

Outcomes based on liver disease



With each liver disease stage there is a stepwise increase in rates of major adverse outcomes including death

Acute hepatic decompensation following CoV-2 infection

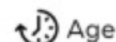


46% of cirrhosis patients decompensate following SARS-CoV-2 infection

22% of those who decompensated had no respiratory symptoms at presentation

Main cause of death: respiratory (secondary: liver)

Major risk factors for mortality:

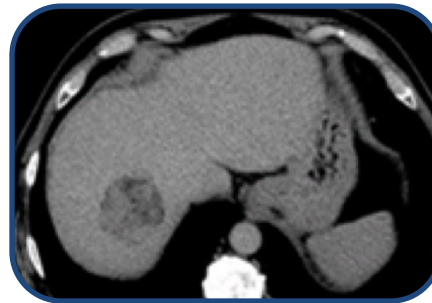
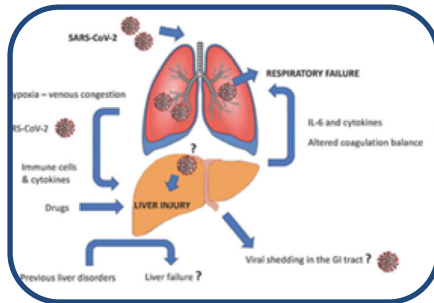


Alcohol related liver disease



Stage of liver disease

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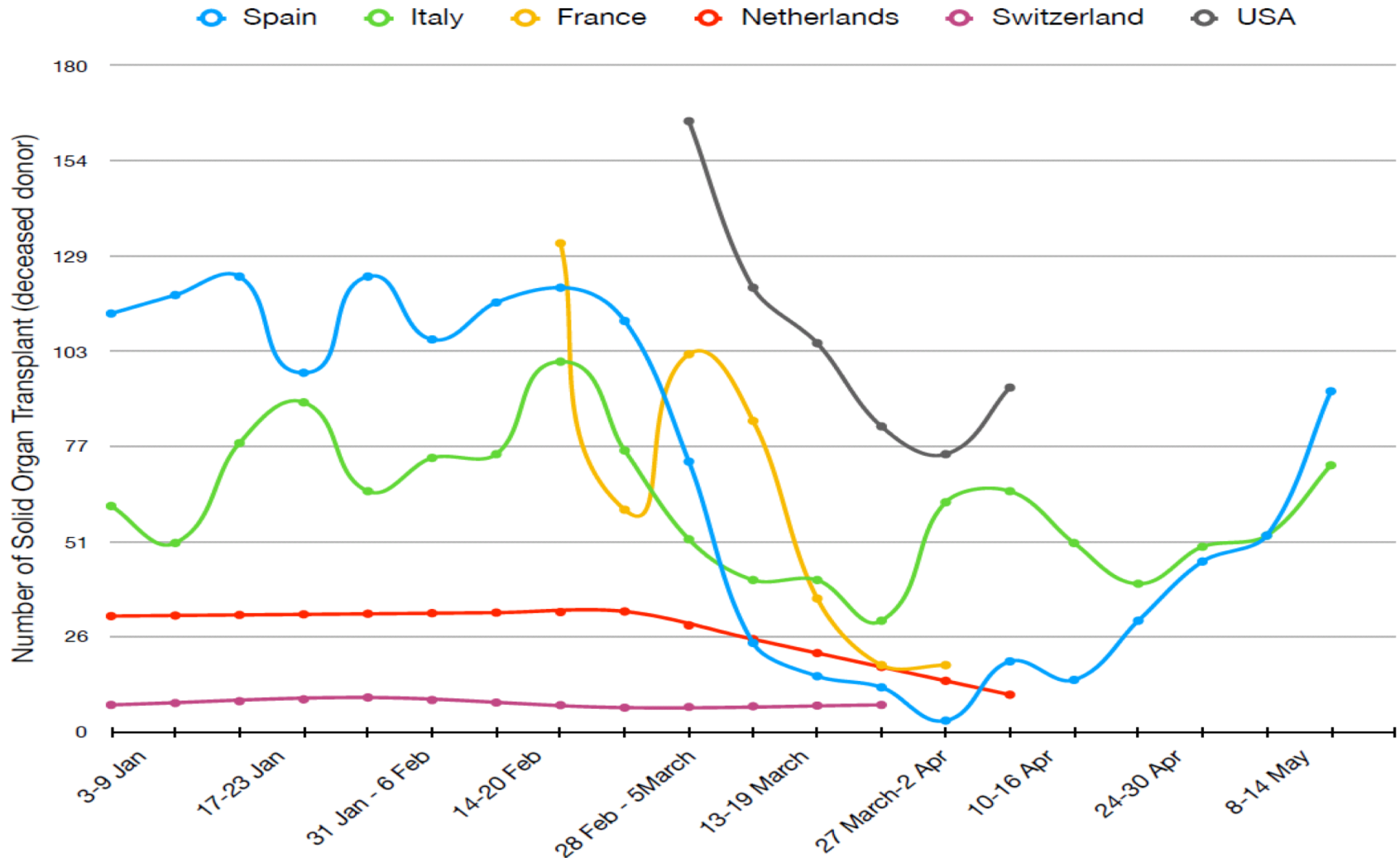


Covid and underlying
CLD (including HCC)

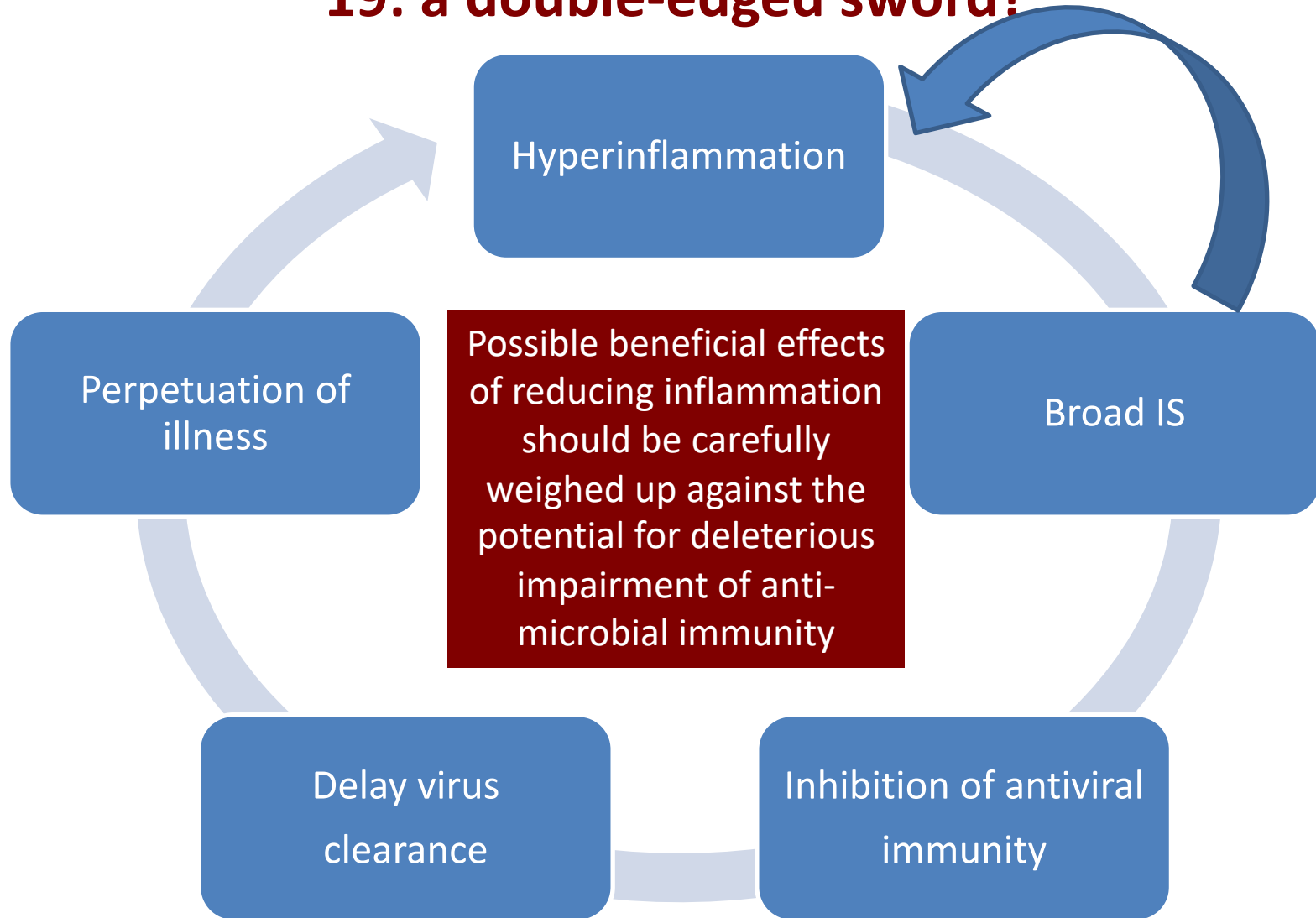


Covid and the LT
patient

Trends of Solid Organ Transplantation (SOT) activity during COVID-19 outbreak in Europe and United States of America

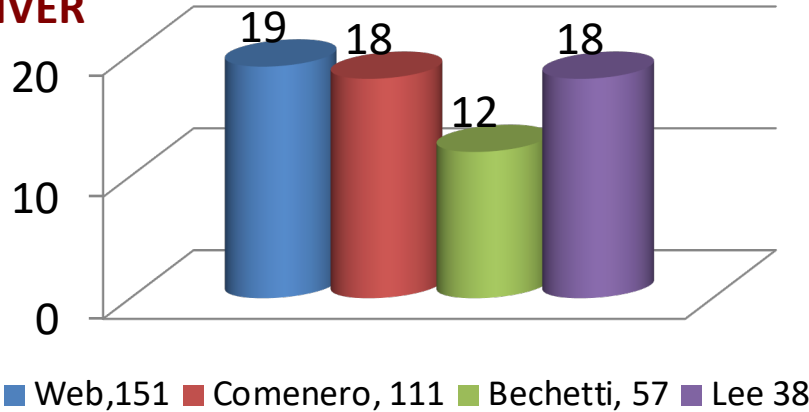


Immunosuppression for hyperinflammation in COVID-19: a double-edged sword?

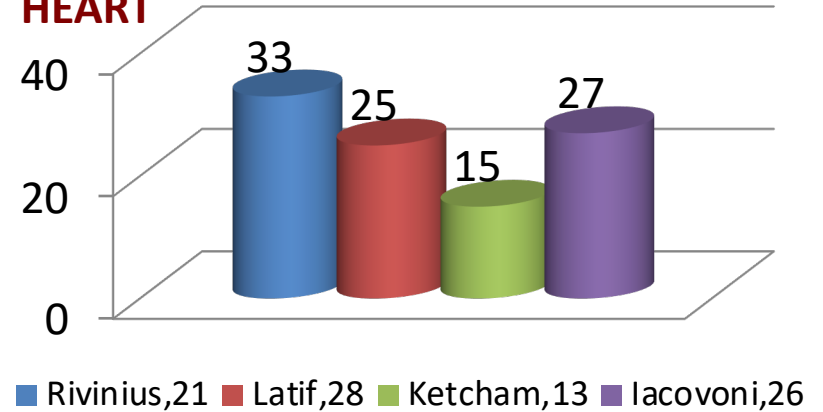


Mortality Rate

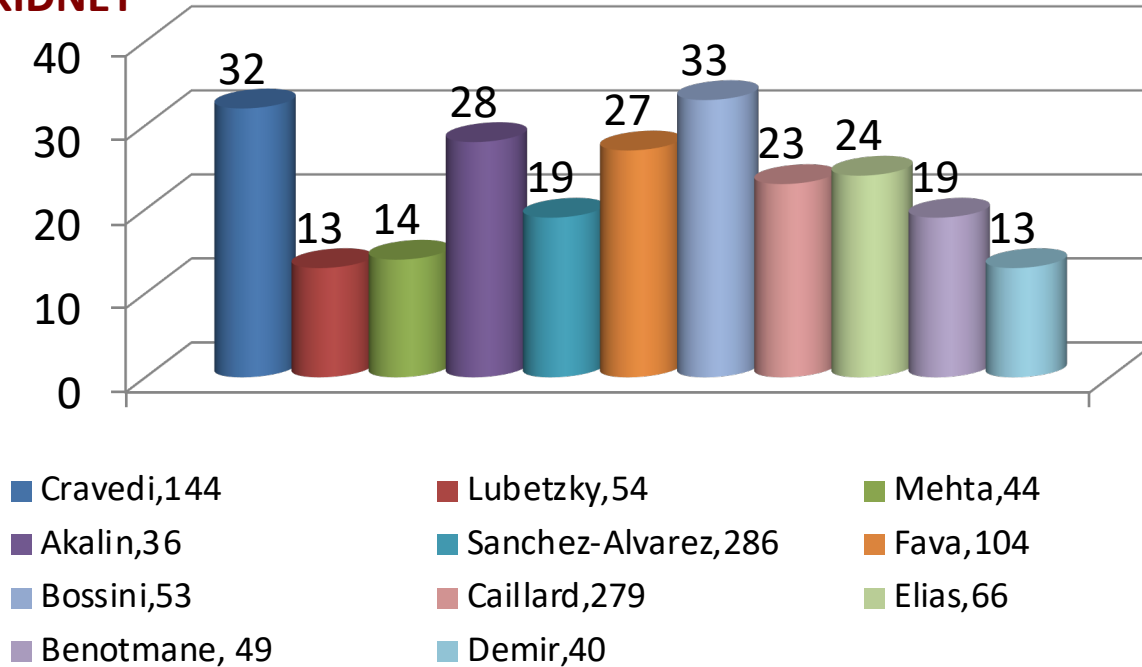
LIVER



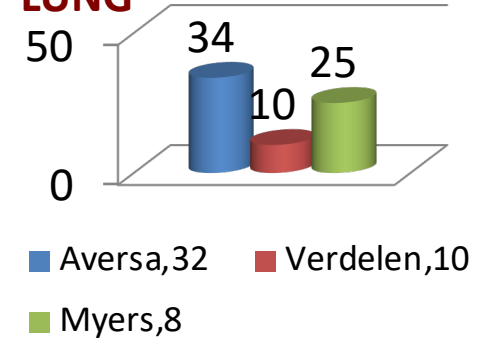
HEART

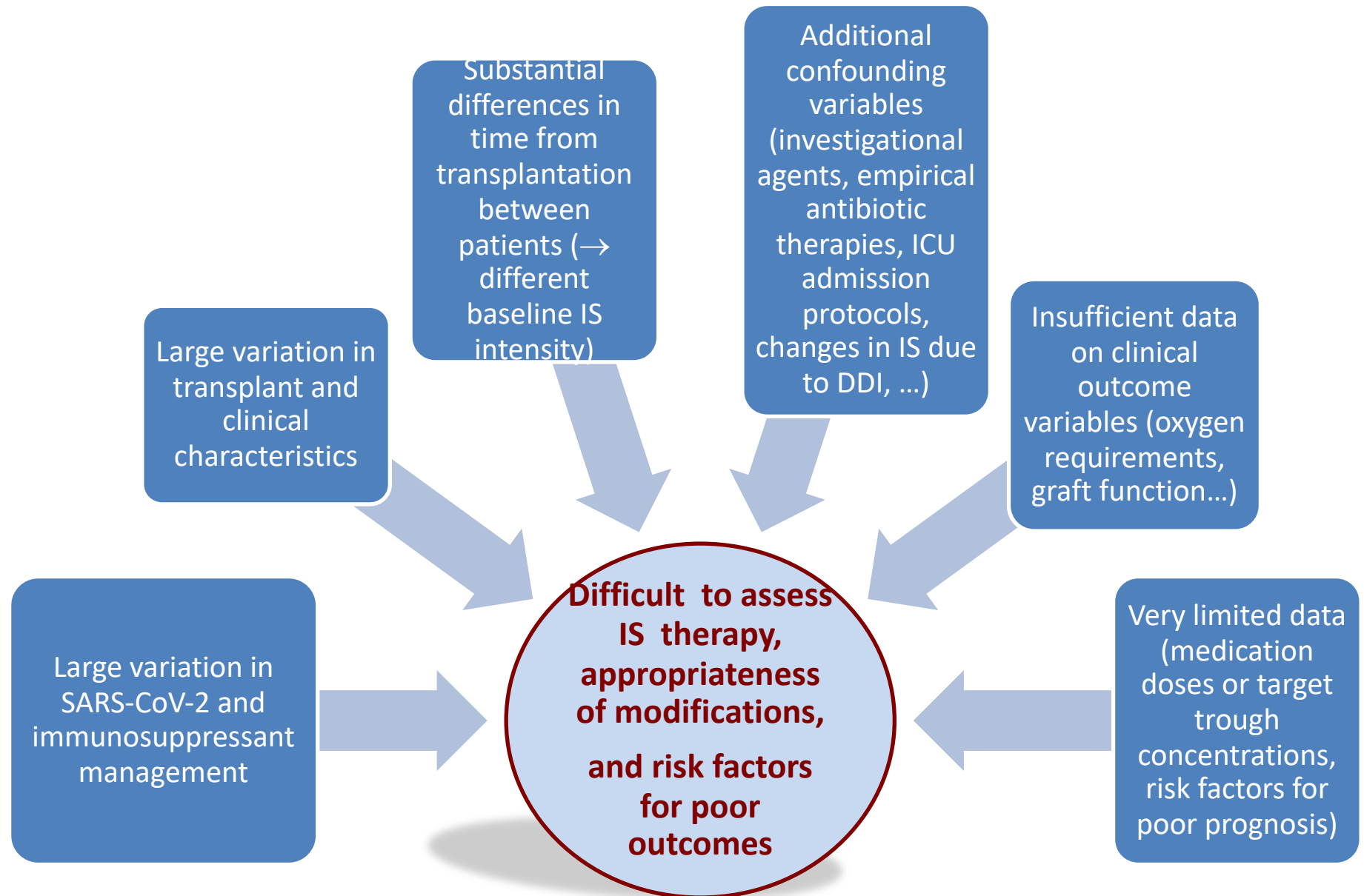


KIDNEY

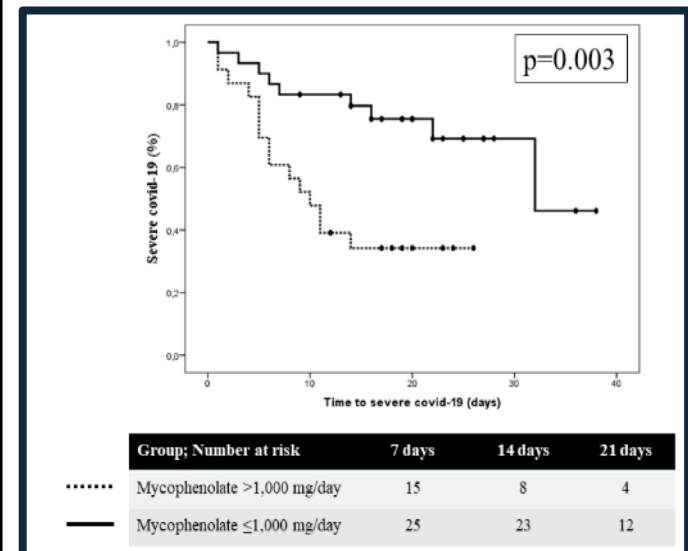
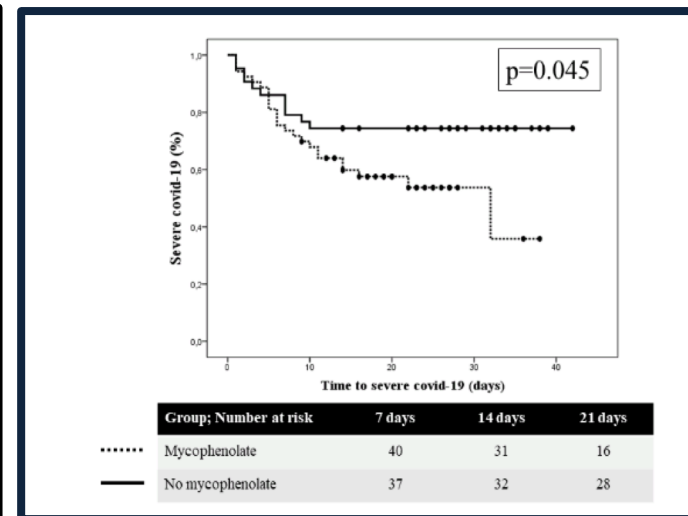
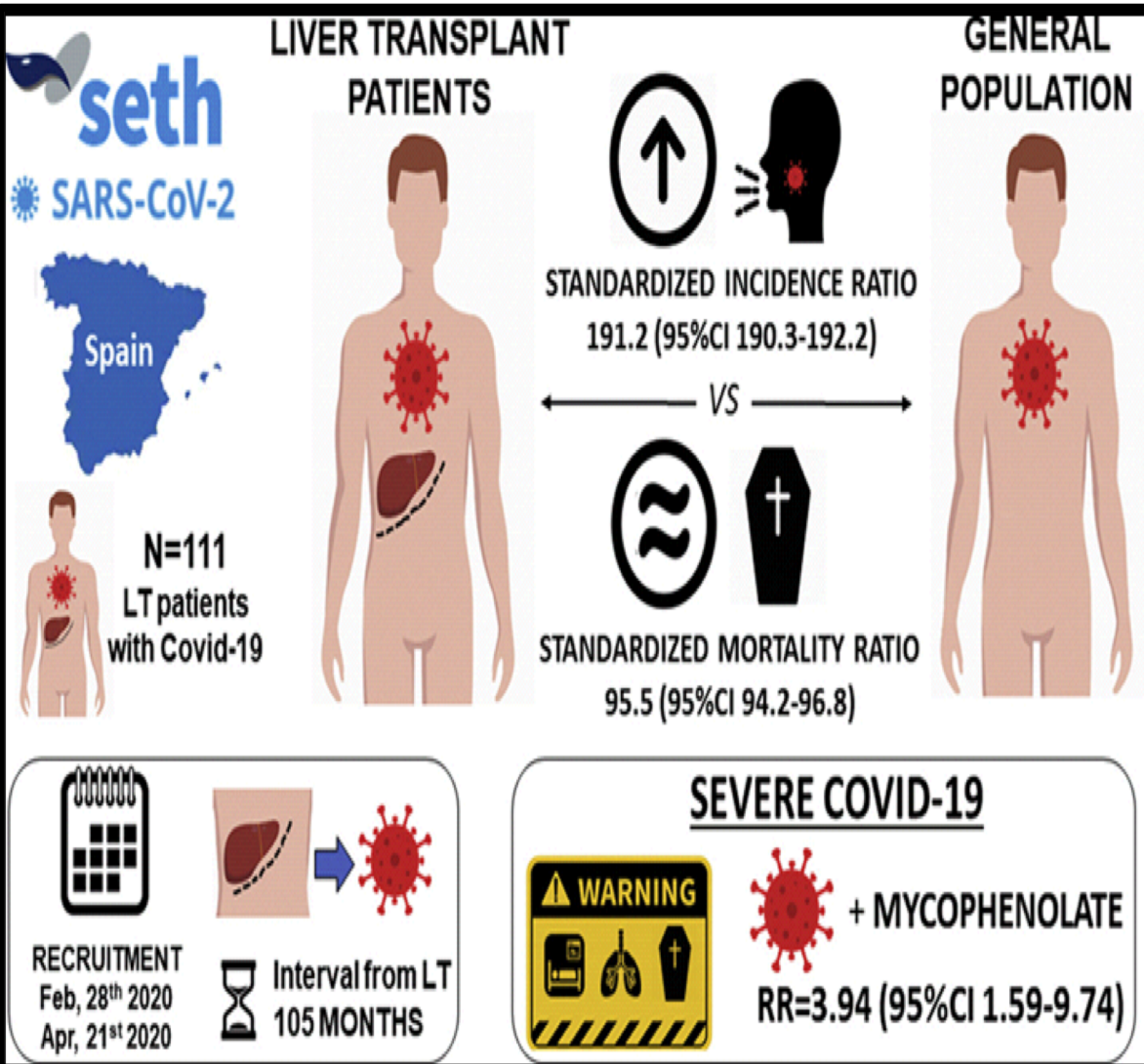


LUNG





COVID-19 in LT patients



Risk factor for poor outcome: IS? Metabolic factors ?

	Long-term liver transplant recipient (>10 years, n=111)	Short-term liver transplant recipient (<2 years, n=40)	p value
Age older than 65 years	55 (50%)	12 (30%)	0.04
Overweight or obesity (body mass index >25 kg/m ²)	89 (80%)	24 (60%)	0.02
Diabetes	67 (60%)	9 (23%)	0.0001
Hyperlipidaemia	50 (45%)	7 (18%)	0.002
Arterial hypertension	111 (100%)	27 (68%)	0.0001
History of cardiovascular event	39 (35%)	2 (5%)	0.0015
Chronic kidney disease	44 (40%)	8 (20%)	0.03
Full immunosuppression*	11 (10%)	28 (70%)	0.0001
COVID-19-related deaths	3 (3%)	0	0.57

COVID-19=coronavirus disease 2019. *Ciclosporin concentration more than 150 ng/mL or tacrolimus concentration more than 5 ng/mL.

Table: Characteristics of liver transplant recipients in Istituto Nazionale Tumori, Milan

Bhoori S et al. *Lancet Gastroenterol Hepatol* 2020

ELITA/ELTR Registry

Mortality was observed only in patients aged 60 years or older (16 [22%, 95% CI 13–33] of 73 patients vs none [0%, 0–13] of 27 patients younger than 60 years),

Although not statistically significant, more patients who were transplanted at least 2 years previously died than did those who received their transplant within the past 2 years (15 [18%, 95% CI 11–28] of 82 patients vs one [5%, 0–24] of 21 patients;

www.thelancet.com/gastrohep

International registry (n=151) *Webb GJ et al; Lancet G&H*

- **Age** (OR 1.68/10yrs; 95%CI 1.02-2.80)
- **Serum creat** (OR 1.56/mg/dl; 1.-2.33)
- **Non-liver cancer** (OR 18.61; 1.94-178.98)

Take home messages

During a pandemic, international collaboration using large-scale registries allows for rapid accumulation of data on well characterised cohorts of patients.

Increasing risk of ICU and death with each liver disease stage (CLD without cirrhosis, CTP-A, CTP-B, CTP-C)

Predominant cause of death is COVID-19 lung disease even in those with acute hepatic decompensation

New decompensation occurs in almost half of patients with cirrhosis, some of which will not have respiratory symptoms at presentation (high suspicion)

Independent risk factors for death in patients with CLD include age, CTP class and alcohol related liver disease

LT recipients are a vulnerable population at high risk of infection. Standardized mortality rates however are similar to those seen in the general population

Independent risk factors for death in LT patients include age and comorbidities.

Most Societies recommend maintaining the same IS therapy . Reduction (MMF) should only be considered under special circumstances .
