
# COVID-19 & Cirrosis Hepática

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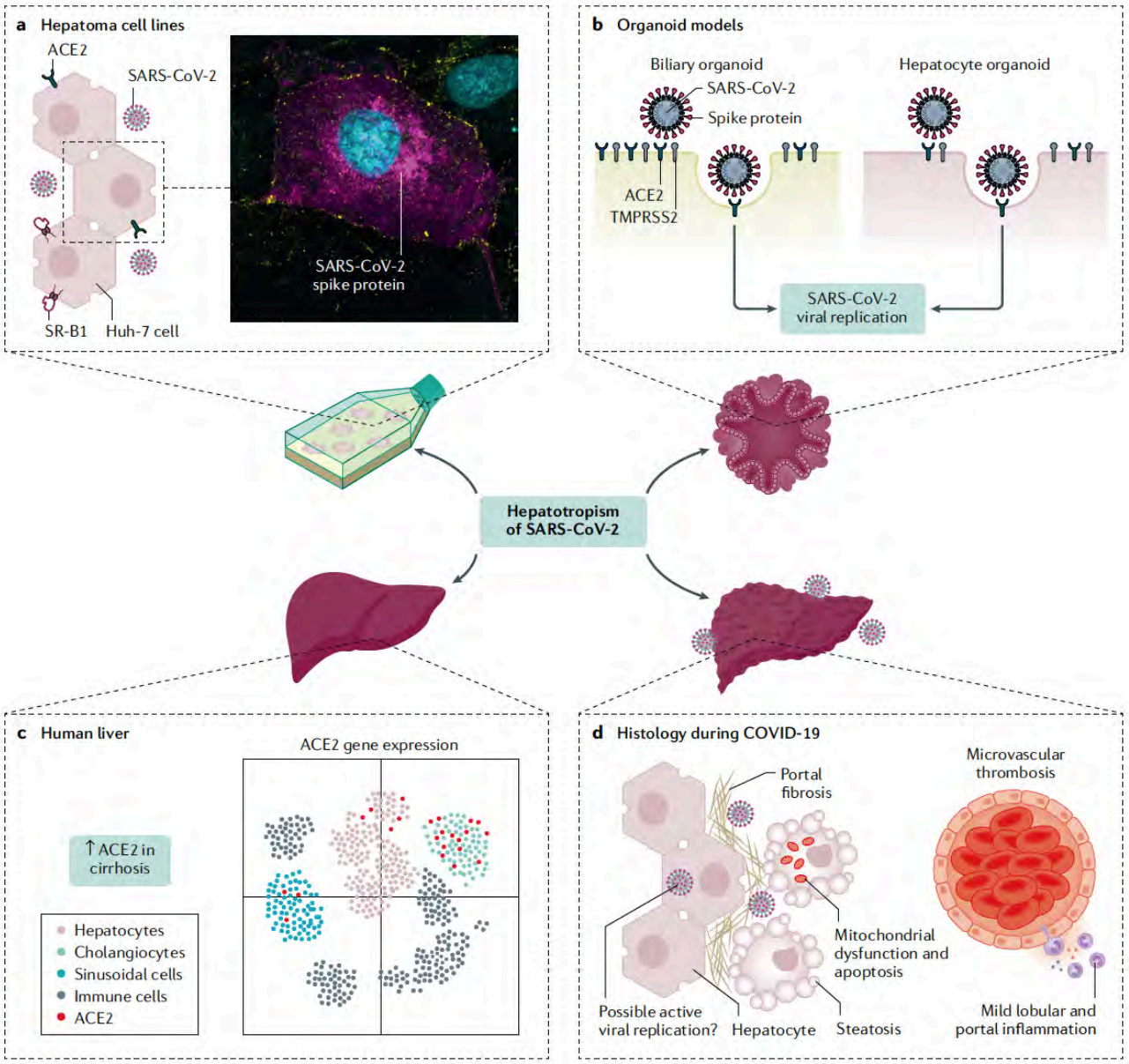
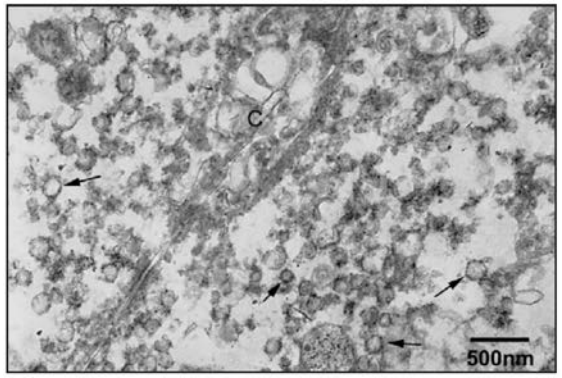
European Reference Network | Hepatological Diseases (ERN RARE-LIVER)

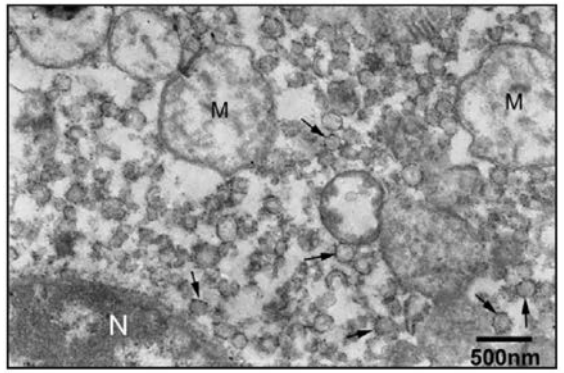
ciberehd

# Hepatotropismo SARS- CoV-2




Coronavirus- like particles in hepatocyte cytoplasm in association with mitochondrial swelling & apoptosis



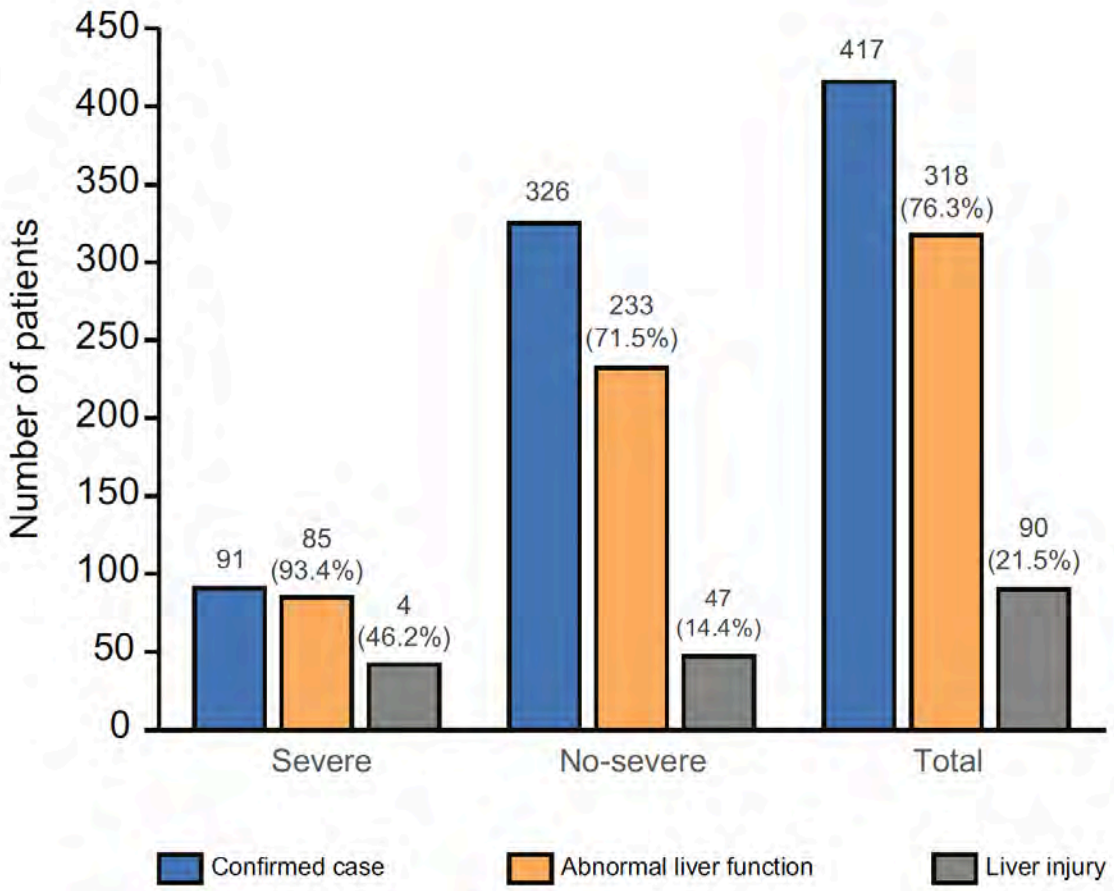



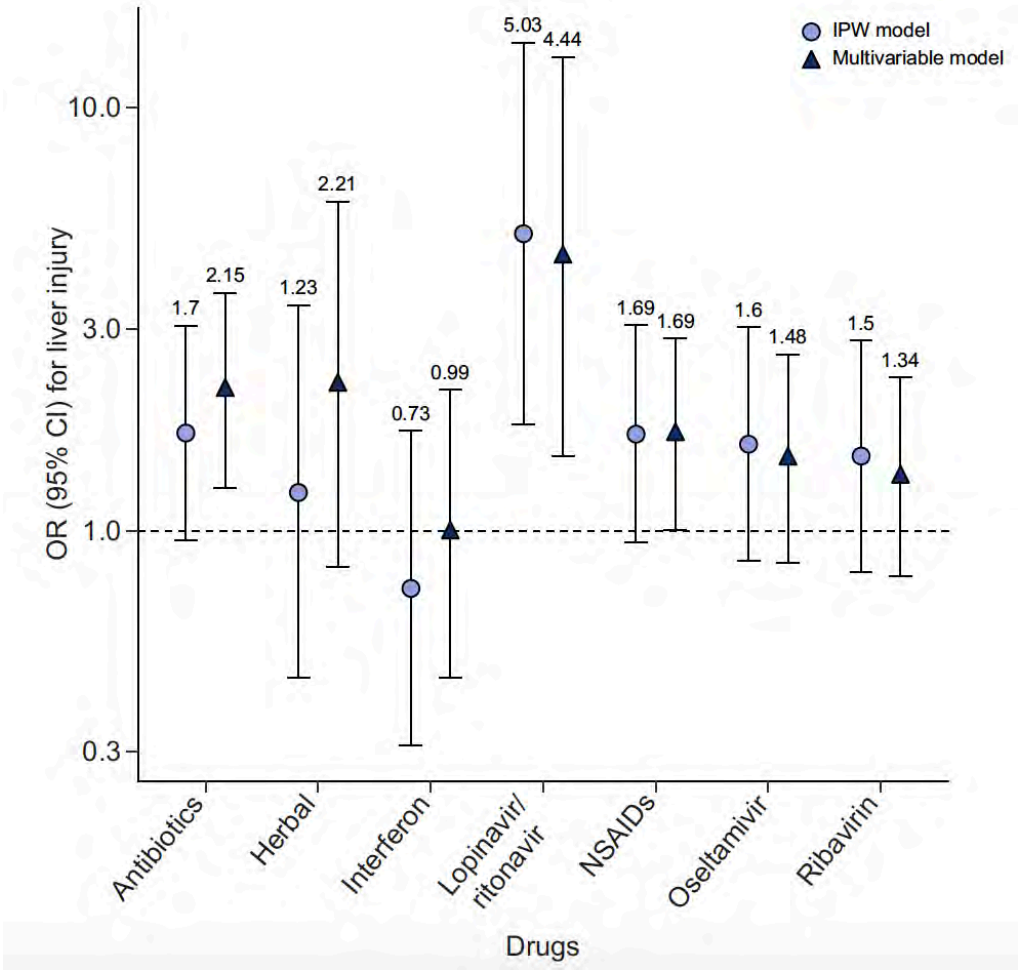

Histological assessment post-mortem liver biopsy from 48 patients dying from severe COVID-19 lung disease:

- vascular abnormalities (100%)
  - portal venous and sinusoidal microthromboses
- microvesicular and macrovesicular steatosis (50%)
- mild portal inflammation (66%)
- portal fibrosis (60%)

Wang Y et al. J Hepatol 2020; Sonzogni A et al. Liver Int 2020

# Daño hepático en pacientes con COVID-19




Estudio con 417 pacientes con COVID-19:

318 (76.3%) alteración PFH*

90 (21.5%) daño hepático durante ingreso

* ALT >40 U/L, AST >40 U/L, GGT >49 U/L, ALP >135 U/L, & total bilirubin >17.1 lmol/L

Cai Q et al. J Hepatol 2020

# Daño hepático en pacientes con COVID-19

**Table 2. Radiographic and Laboratory Findings.***

| Variable | All Patients (N=1099) | Disease Severity | |
|---|---|---|---|
| | | Nonsevere (N=926) | Severe (N=173) |
| Platelet count | | | |
| Median (IQR) — per $mm^3$ | 168,000 (132,000–207,000) | 172,000 (139,000–212,000) | 137,500 (99,000–179,500) |
| Distribution — no./total no. (%) | | | |
| <150,000 per $mm^3$ | 315/869 (36.2) | 225/713 (31.6) | 90/156 (57.7) |
| Median hemoglobin (IQR) — g/dl‡ | 13.4 (11.9–14.8) | 13.5 (12.0–14.8) | 12.8 (11.2–14.1) |
| Distribution of other findings — no./total no. (%) | | | |
| C-reactive protein ≥10 mg/liter | 481/793 (60.7) | 371/658 (56.4) | 110/135 (81.5) |
| Procalcitonin ≥0.5 ng/ml | 35/633 (5.5) | 19/516 (3.7) | 16/117 (13.7) |
| Lactate dehydrogenase ≥250 U/liter | 277/675 (41.0) | 205/551 (37.2) | 72/124 (58.1) |
| Aspartate aminotransferase >40 U/liter | 168/757 (22.2) | 112/615 (18.2) | 56/142 (39.4) |
| Alanine aminotransferase >40 U/liter | 158/741 (21.3) | 120/606 (19.8) | 38/135 (28.1) |
| Total bilirubin >17.1 μmol/liter | 76/722 (10.5) | 59/594 (9.9) | 17/128 (13.3) |
| Creatine kinase ≥200 U/liter | 90/657 (13.7) | 67/536 (12.5) | 23/121 (19.0) |
| Creatinine ≥133 μmol/liter | 12/752 (1.6) | 6/614 (1.0) | 6/138 (4.3) |
| D-dimer ≥0.5 mg/liter | 260/560 (46.4) | 195/451 (43.2) | 65/109 (59.6) |

Alteracion transitoria
No casos IHAG

¿Efecto citopatico directo del virus?
Sepsis grave, inestabilidad hemodinamica, ventilacion mecanica…

¿Tiene valor pronóstico?
Resultados controvertidos en la asociacion citolisis y mortalidad

Guan W et al. N Engl J Med 2020

Research Article
Cirrhosis and Liver Failure

JOURNAL OF HEPATOLOGY

# Outcomes following SARS-CoV-2 infection in patients with chronic liver disease: An international registry study

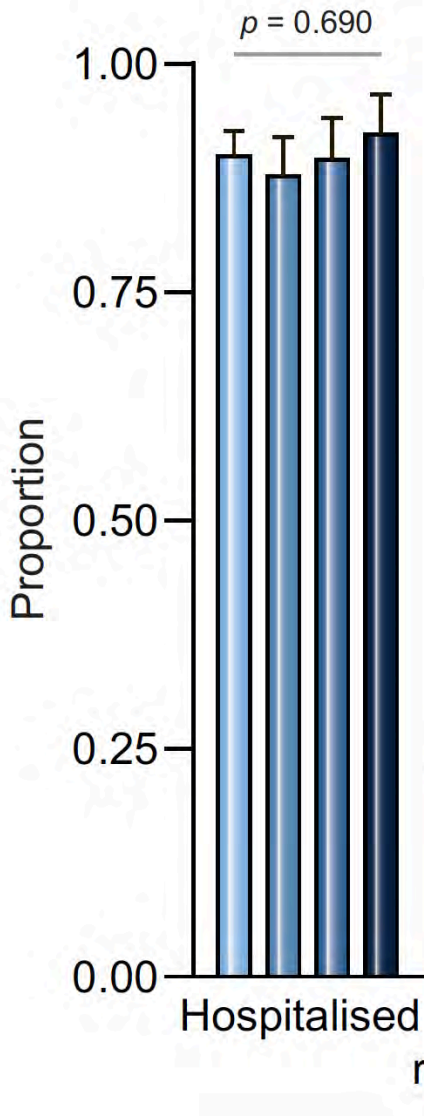
Thomas Marjot[1,*,†], Andrew M. Moon[2,†], Jonathan A. Cook[3], Sherief Abd-Elsalam[4], Costica Aloman[5], Matthew J. Armstrong[6], Elisa Pose[7,8], Erica J. Brenner[9], Tamsin Cargill[1], Maria-Andreea Catana[10], Renumathy Dhanasekaran[11], Ahad Eshraghian[12], Ignacio García-Juárez[13], Upkar S. Gill[14], Patricia D. Jones[15], James Kennedy[1], Aileen Marshall[16], Charmaine Matthews[17], George Mells[18], Carolyn Mercer[1], Ponni V. Perumalswami[19], Emma Avitabile[7], Xialong Qi[20], Feng Su[21], Nneka N. Ufere[22], Yu Jun Wong[23], Ming-Hua Zheng[24,25], Eleanor Barnes[1,†], Alfred S. Barritt IV,[2,†], Gwilym J. Webb[1,18,†]

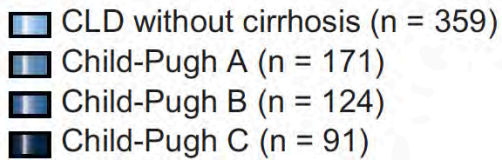
745 pacientes con CLD & SARS-CoV-2
386 con cirrosis
359 sin cirrosis
(2 registros internacionales US & EU)

643 pacientes con SARS-CoV-2
(Oxford University Hospitals NHS Foundation Trust)

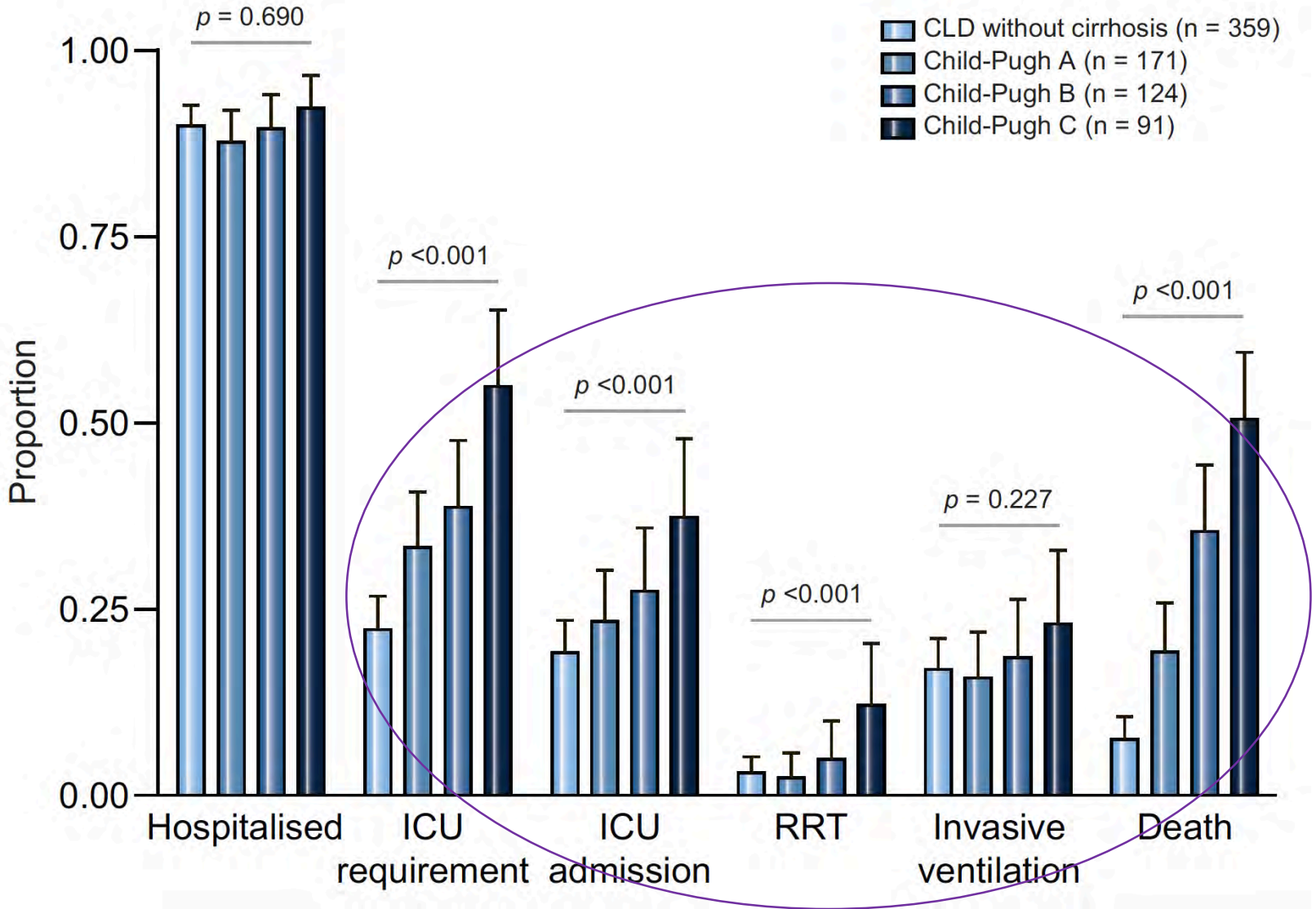
# Infección por SARS-CoV2 & enfermedad hepática

No diferencias tasa hospitalizacion



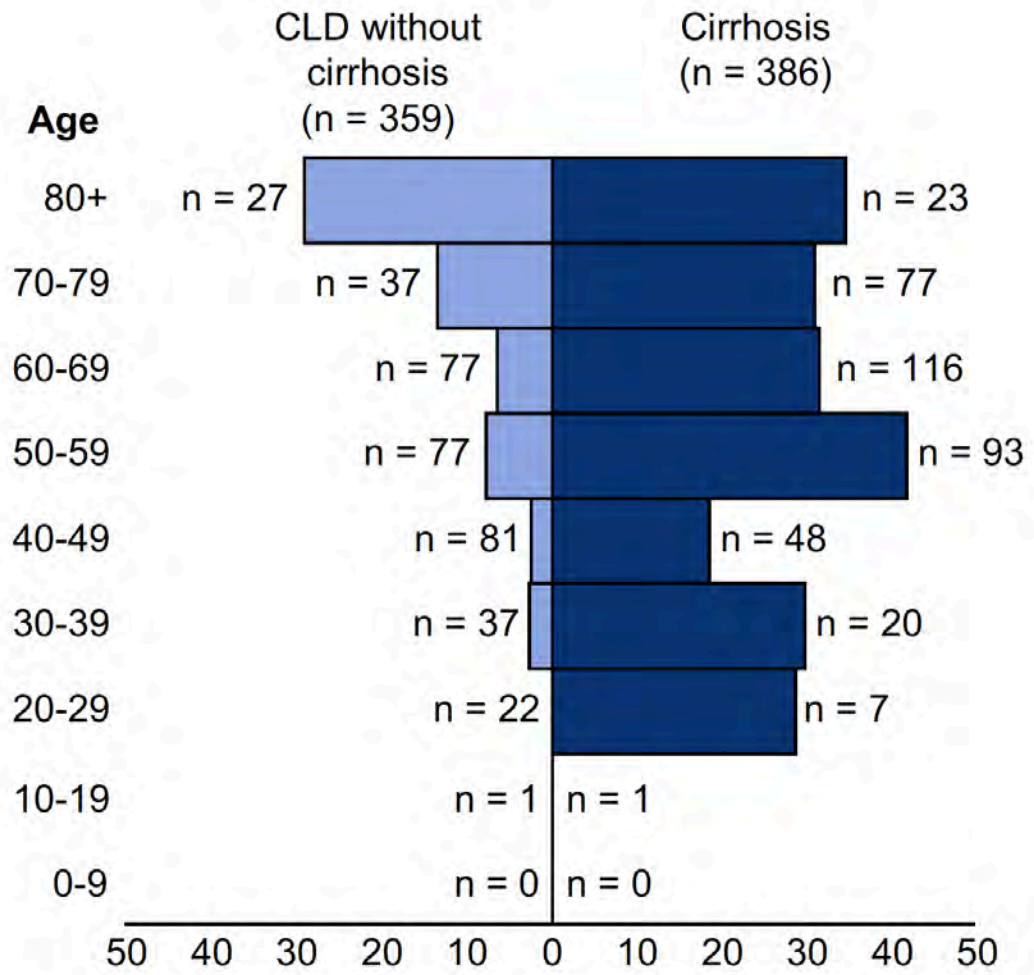



# Infección por SARS-CoV2 & enfermedad hepática



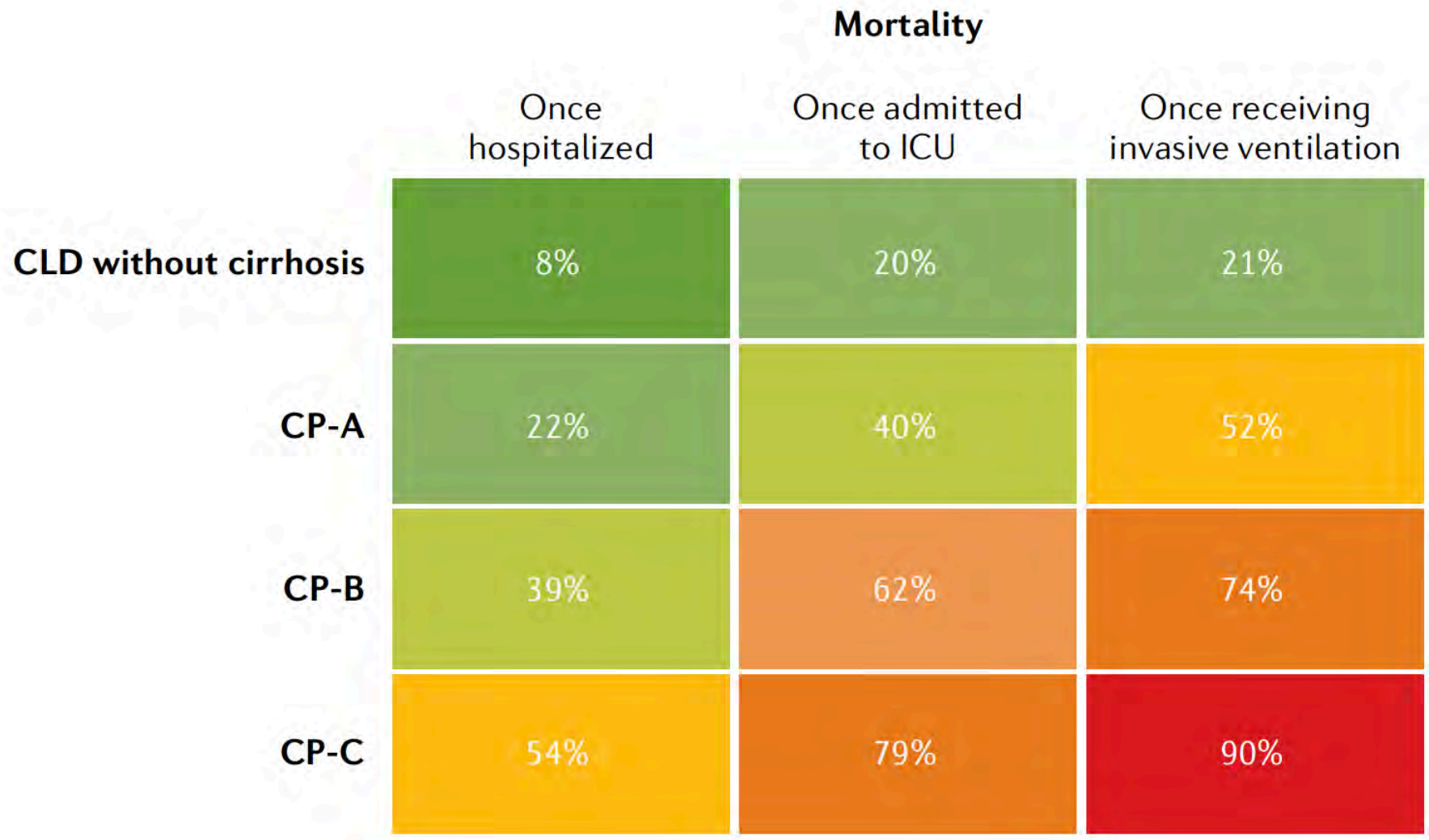

Mayor tasa de:
Requerimiento UCI
Tec. depuracion renal
Ventilación invasiva
Muerte

# Infección por SARS-CoV2 & enfermedad hepática



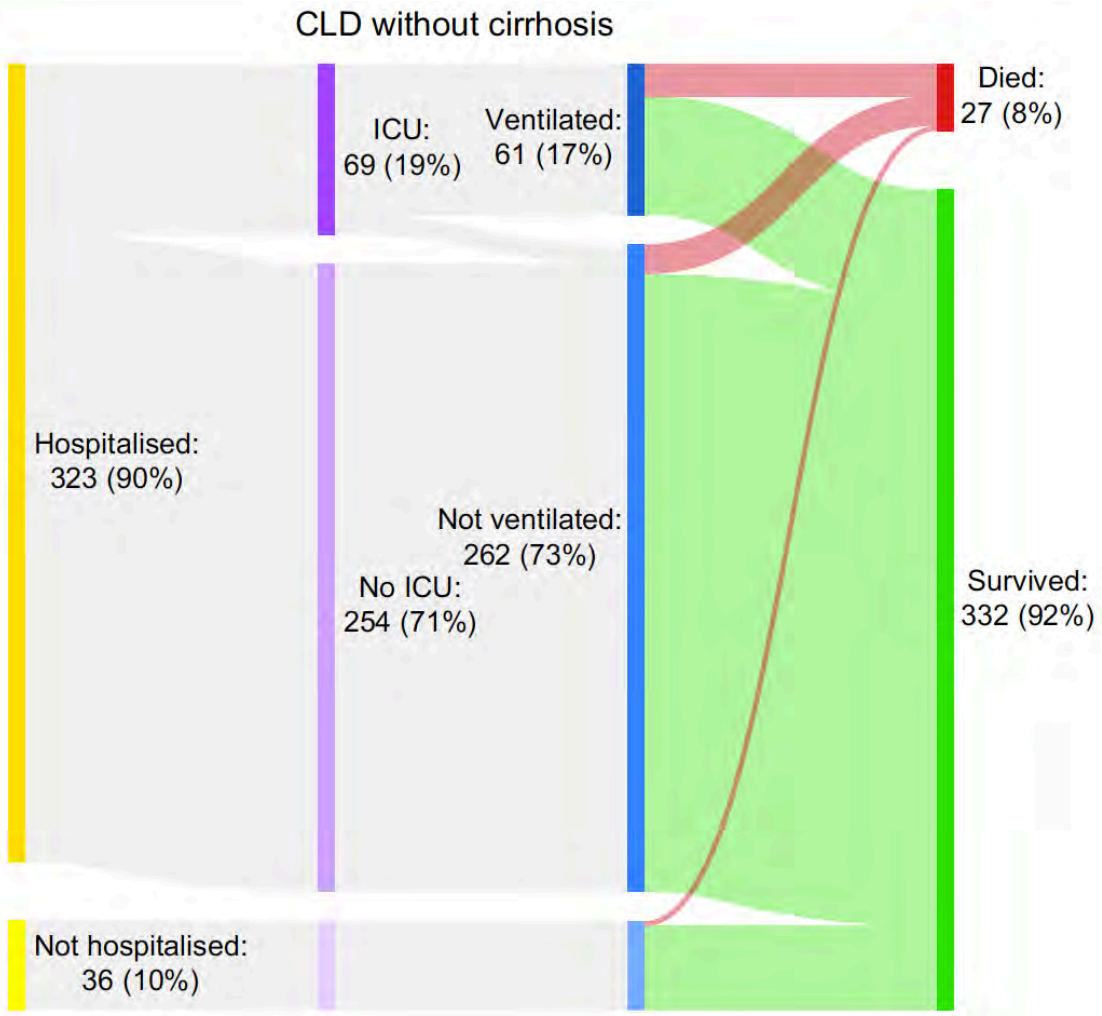

Mortalidad por franja de edad

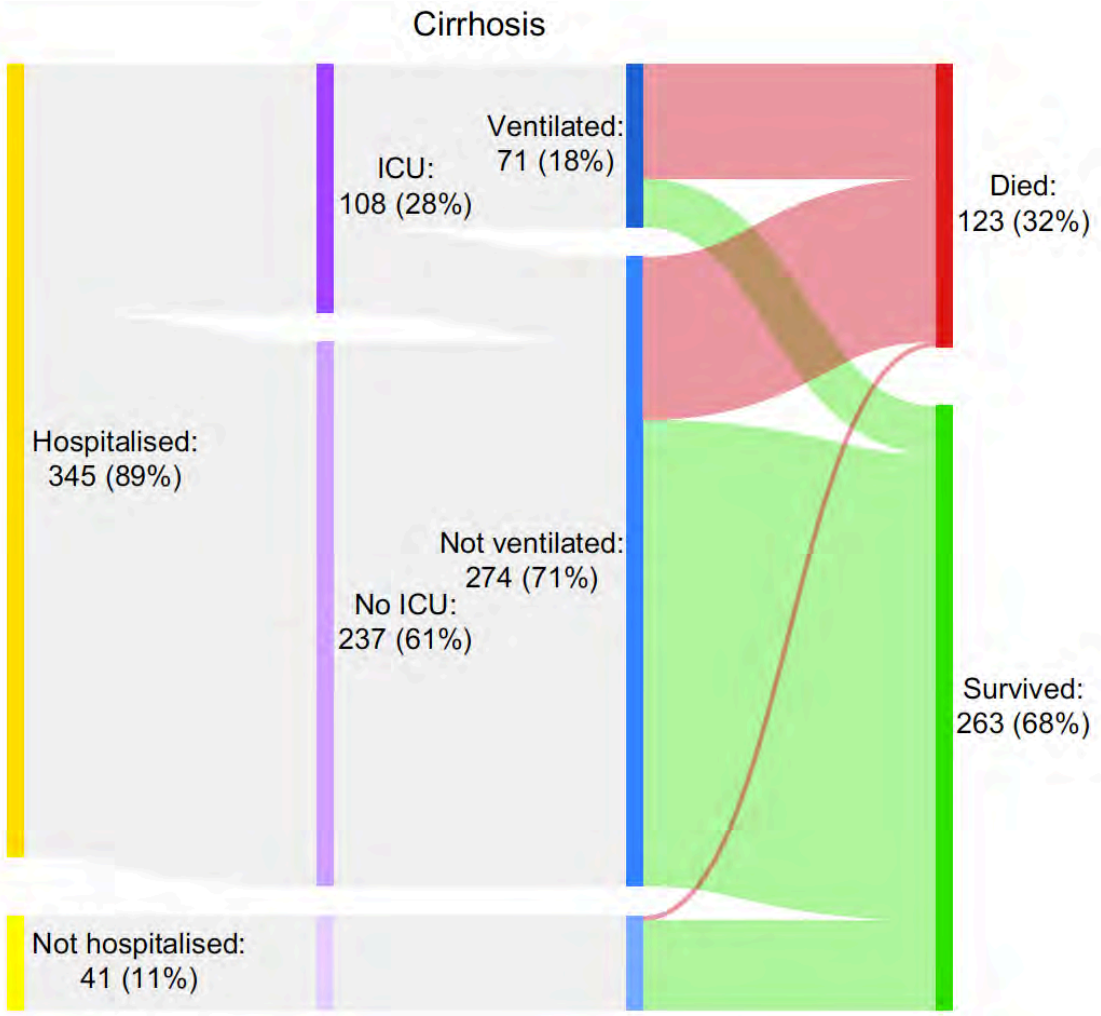
# Infección por SARS-CoV2 & enfermedad hepática




Marjot T et al. Nat Rev Gastroenterol Hepatol 2021

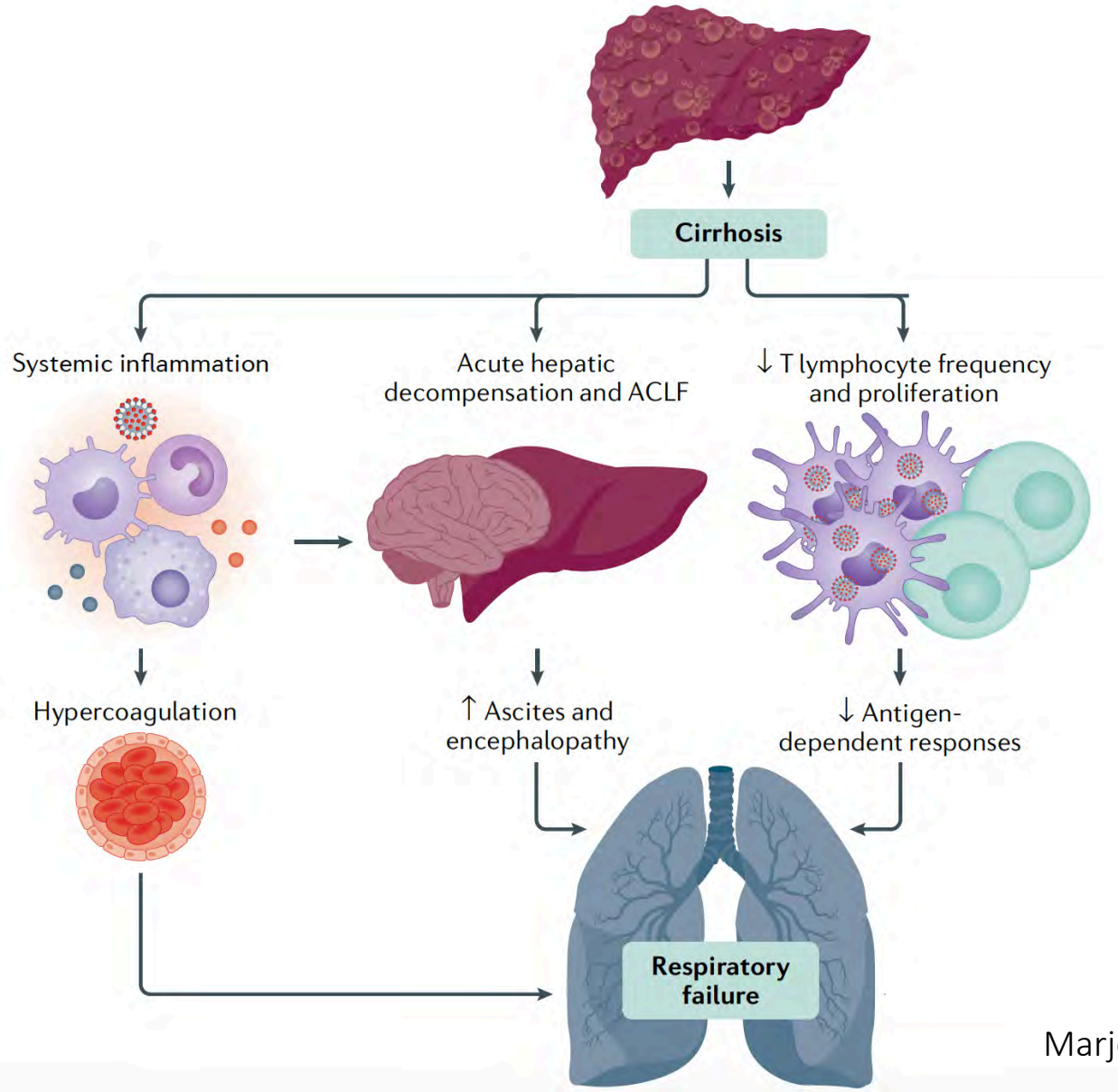
# Curso clínico de la infección SARS-CoV-2 en CLD



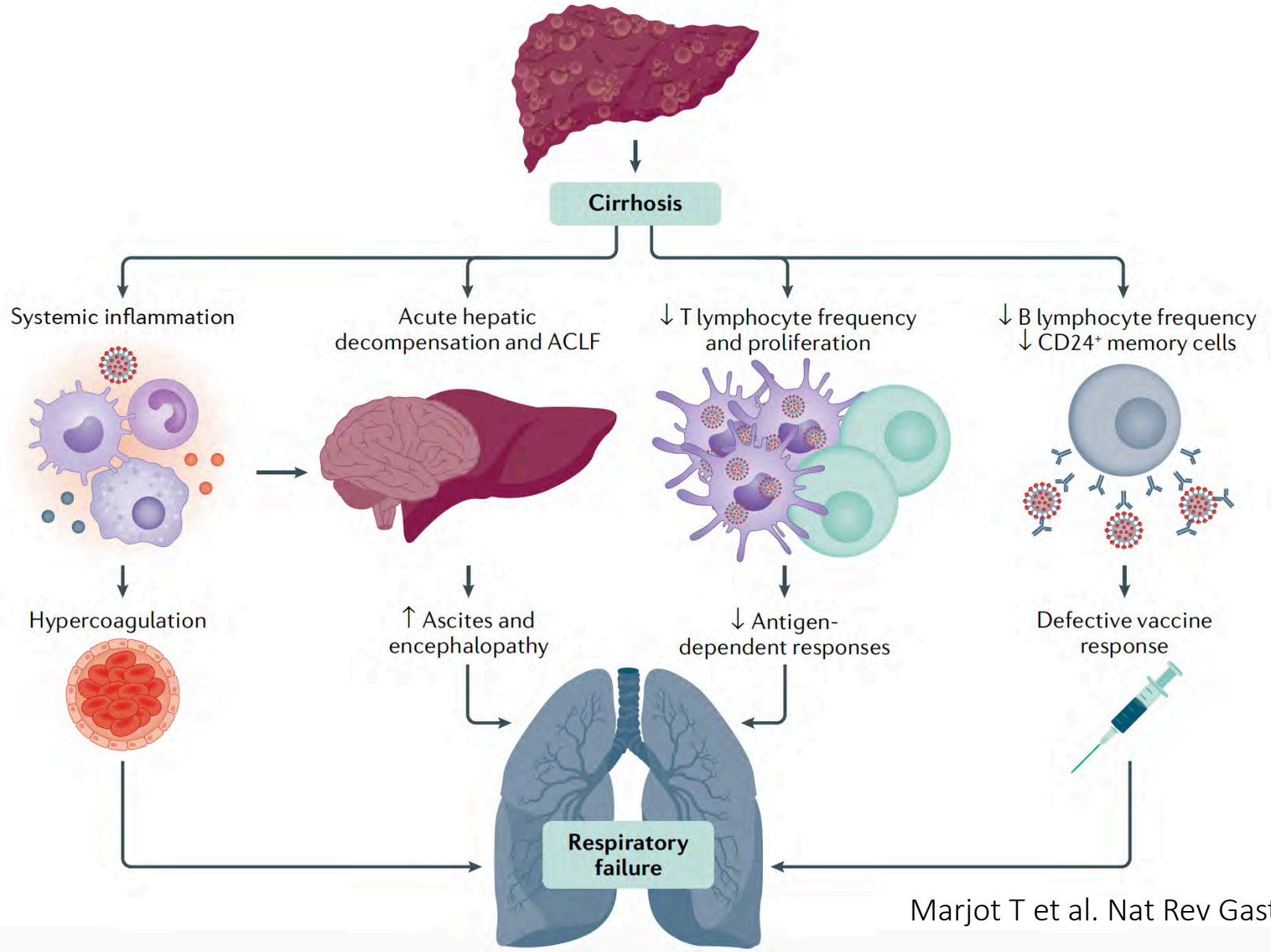
| Study | Design | Country/region and number included | Major findings |
|---|---|---|---|
| *Cirrhosis* | | | |
| Marjot et al.[91] (Oct 2020) | Large international registry study | 29 countries; SARS-CoV-2 infection plus cirrhosis ($n=386$); SARS-CoV-2 plus CLD without cirrhosis ($n=359$); SARS-CoV-2 plus non-CLD ($n=620$) | Overall mortality: CP-A (19%), CP-B (35%), CP-C (51%), CLD without cirrhosis (8%); increased risk of death cirrhosis vs CLD without cirrhosis: CP-A (OR 1.9, 95% CI 1.03–3.5), CP-B (OR 4.1, 95% CI 2.4–7.77), CP-C (OR 9.32, 95% CI 4.80–18); increased risk of death compared with propensity score-matched patients without CLD: CP-B (+20%, 8.8–31.3%) and CP-C (+38%, 27.1–49.2%) |
| Iavarone et al.[93] (Jun 2020) | Multicentre retrospective cohort study | Italy; SARS-CoV-2 plus cirrhosis ($n=50$); SARS-CoV-2 plus no cirrhosis ($n=399$); cirrhosis plus bacterial infection ($n=47$) | 30-day mortality: SARS-CoV-2 plus cirrhosis vs SARS-CoV-2 plus no cirrhosis (34% vs 18%; $P=0.030$); SARS-CoV-2 plus cirrhosis vs cirrhosis plus bacterial infection (34% vs 17%; $P=0.03$) |
| Bajaj et al.[177] (Jun 2020) | Multicentre retrospective cohort study | North America and Canada; SARS-CoV-2 plus no cirrhosis ($n=108$); SARS-CoV-2 plus cirrhosis ($n=37$); cirrhosis alone ($n=127$) | Overall mortality: cirrhosis plus SARS-CoV-2 higher mortality compared with patients with SARS-CoV-2 alone (30% vs 13%; $P=0.03$) but not between patients with cirrhosis plus SARS-CoV-2 and patients with cirrhosis alone (30% vs 20%; $P=0.16$) |
| Kim et al.[178] (Sep 2020) | Multicentre retrospective cohort study | North America; SARS-CoV-2 plus CLD without cirrhosis ($n=620$); SARS-CoV-2 plus cirrhosis ($n=227$) | Increased risk of death with decompensated cirrhosis (OR 2.91, 95% CI 1.70–5.00); no increased risk with compensated cirrhosis (OR 0.83, 95% CI 0.46–1.49) |
| Sarin et al.[179] (Jun 2020) | Multinational registry study | 13 countries in Asia; SARS-CoV-2 plus CLD without cirrhosis ($n=185$); SARS-CoV-2 plus cirrhosis ($n=43$) | Overall mortality: SARS-CoV-2 plus CLD without cirrhosis vs SARS-CoV-2 plus cirrhosis (16% vs 3%; $P=0.002$) |
| Clift et al.[128] (Sep 2020) | Population-based cohort study using electronic health record data | United Kingdom; 6 million adults: 11,865 with cirrhosis, 37 deaths from COVID-19 in patients with cirrhosis and 106 hospitalizations with COVID-19 in patients with cirrhosis | Hazard ratio for COVID-19-related mortality in patients with cirrhosis: women in derivation cohort, 1.8 (95% CI 1.15–2.99); men in derivation cohort, 1.29 (95% CI 0.83–2.02) |
| Ioannou et al.[83] (Nov 2020) | Population-based study using electronic health record data | North America; SARS-CoV-2 plus cirrhosis ($n=305$); SARS-CoV-2 plus no cirrhosis ($n=9,826$); cirrhosis alone ($n=3,301$) | Patients with SARS-CoV-2 plus cirrhosis 3.5 times more likely to die than those with SARS-CoV-2 without cirrhosis |

# Possible mechanisms for adverse CoVID-19 outcomes in cirrhosis




Marjot T et al. Nat Rev Gastroenterol Hepatol 2021

# Possible mechanisms for adverse CoVID-19 outcomes in cirrhosis




Marjot T et al. Nat Rev Gastroenterol Hepatol 2021

# Vacunas y cirrosis

Table. SARS-CoV-2 Vaccines

| Vaccine | Manufacturer | Vaccine type | Antigen | Dose | Dosage | Storage conditions | Efficacy against severe COVID-19[a] | Overall efficacy | Current approvals |
|---|---|---|---|---|---|---|---|---|---|
| mRNA-1273 | Moderna (US) | mRNA | Full-length spike (S) protein with proline substitutions | 100 µg | 2 Doses 28 d apart | −25° to −15 °C; 2-8 °C for 30 d; room temperature ≤12 h | 100% 14 d After second dose (95% CI, not estimable to 1.00) | 92.1% 14 d After 1 dose (95% CI, 68.8%-99.1%); 94.1% 14 d after second dose (95% CI, 89.3%-96.8%) | EUA: the US, EU, Canada, and UK |
| BNT162b2 | Pfizer-BioNTech (US) | mRNA | Full-length S protein with proline substitutions | 30 µg | 2 Doses 21 d apart | −80° to −60 °C; 2-8 °C for 5 d; room temperature ≤2 h | 88.9% After 1 dose (95% CI, 20.1%-99.7%) | 52% After 1 dose (95% CI, 29.5%-68.4%); 94.6% 7 d after second dose (95% CI, 89.9%-97.3%) | EUA: the US, EU, Canada, and UK |
| Ad26.CoV2.S | Janssen/ Johnson & Johnson (US) | Viral vector | Recombinant, replication-incompetent human adenovirus serotype 26 vector encoding a full-length, stabilized SARS-CoV-2 S protein | $5 \times 10^{10}$ Viral particles | 1 Dose | −20 °C; 2-8 °C for 3 mo | 85% After 28 d; 100% after 49 d | 72% in the US; 66% in Latin America; 57% in South Africa (at 28 d) | EUA: the US, EU, and Canada |
| ChAdOx1 (AZS1222) | AstraZeneca/ Oxford (UK) | Viral vector | Replication-deficient chimpanzee adenoviral vector with the SARS-CoV-2 S protein | $5 \times 10^{10}$ Viral particles (standard dose) | 2 Doses 28 d apart (intervals >12 wk studied) | 2-8 °C for 6 mo | 100% 21 d After first dose | 64.1% After 1 dose (95% CI, 50.5%-73.9%); 70.4% 14 d after second dose (95% CI, 54.8%-80.6%) | EUA: WHO/Covax, the UK, India, and Mexico |
| NVX-CoV2373 | Novavax, Inc (US) | Protein subunit | Recombinant full-length, prefusion S protein | 5 µg of protein and 50 µg of Matrix-M adjuvant | 2 Doses | 2-8 °C for 6 mo | Unknown | 89.3% in the UK after 2 doses (95% CI, 75.2%-95.4%); 60% in South Africa (95% CI, 19.9%-80.1%) | EUA application planned |
| CVnCoV | CureVac/ GlaxoSmithKline (Germany) | mRNA | Prefusion stabilized full-length S protein of the SARS-CoV-2 virus | 12 µg | 2 Doses 28 d apart | 2-8 °C for 3 mo; room temperature for 24 h | Unknown | Phase 3 trial ongoing | |
| Gam-COVID-Vac (Sputnik V) | Gamaleya National Research Center for Epidemiology and Microbiology (Russia) | Viral vector | Full-length SARS-CoV-2 glycoprotein S carried by adenoviral vectors | $10^{11}$ Viral particles per dose for each recombinant adenovirus | 2 Doses (first, rAd26; second, rAd5) 21 d apart | −18 °C (Liquid form); 2-8 °C (freeze dried) for up to 6 mo | 100% 21 d After first dose (95% CI, 94.4%-100%) | 87.6% 14 d After first dose (95% CI, 81.1%-91.8%); 91.1% 7 d after second dose (95% CI, 83.8%-95.1%) | EUA: Russia, Belarus, Argentina, Serbia, UAE, Algeria, Palestine, and Egypt |
| CoronaVac | Sinovac Biotech (China) | Inactivated virus | Inactivated CN02 strain of SARS-CoV-2 created from Vero cells | 3 µg With aluminum hydroxide adjuvant | 2 Doses 14 d apart | 2-8 °C; Lifespan unknown | Unknown | Phase 3 data not published; reported efficacy 14 d after dose 2: 50.38% (mild) and 78% (mild to severe) in Brazil, 65% in Indonesia, and 91.25% in Turkey | EUA: China, Brazil, Columbia, Bolivia, Brazil, Chile, Uruguay, Turkey, Indonesia, and Azerbaijan |
| BBIBP-CorV | Sinopharm 1/2 (China) | Inactivated virus | Inactivated HB02 strain of SARS-CoV-2 created from Vero cells | 4 µg With aluminum hydroxide adjuvant | 2 Doses 21 d apart | 2-8 °C; Lifespan unknown | Unknown | Phase 3 data not published; unpublished reports of 79% and 86% efficacy | EUA: China, UAE, Bahrain, Serbia, Peru, and Zimbabwe |

Abbreviations: EUA, Emergency Use Authorization; UAE, United Arab Emirates; WHO, World Health Organization.

[a] Efficacy against severe disease, which includes COVID-19–related hospitalization, varies by age and by time after vaccination.

# Vacunas y cirrosis

Cirrosis: inflamacion sistemica y disfuncion inmune innata/adaptativa
Respuesta alterada a vacunas (neumococo, hepatitis B)
Respuesta a la vacuna en cirrosis (inmunidad humoral y celular)?

EASL™ The Home of Hepatology | COVID-HEP COVID-19 in Patients with Liver Disease or Transplantation REGISTRY 2.0

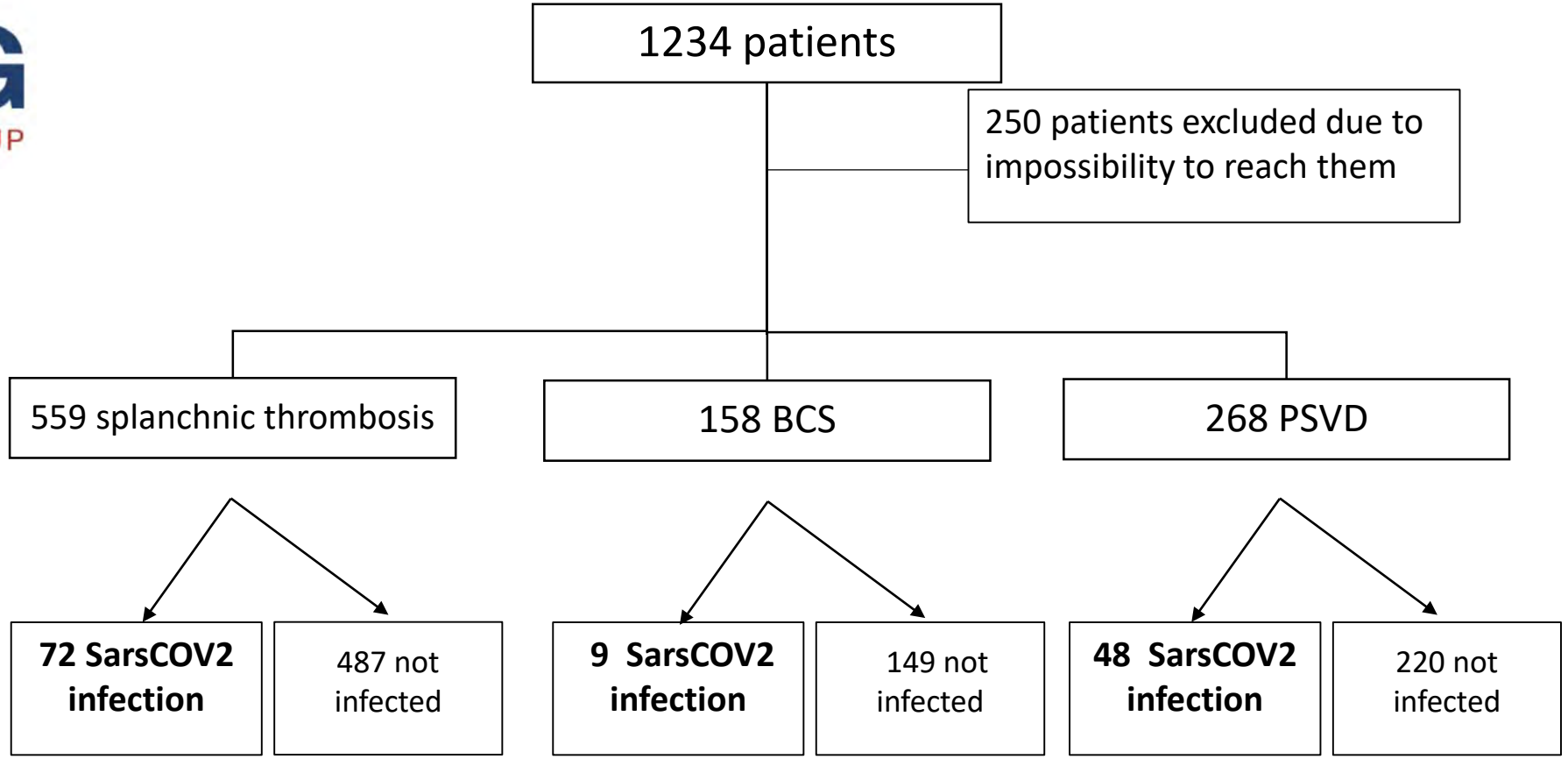
AASLD AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

SECURE-Liver REGISTRY Surveillance Epidemiology of Coronavirus (COVID-19) Under Research Exclusion

# Infección por SARS-CoV2 & Enfermedad Vascular Hepática

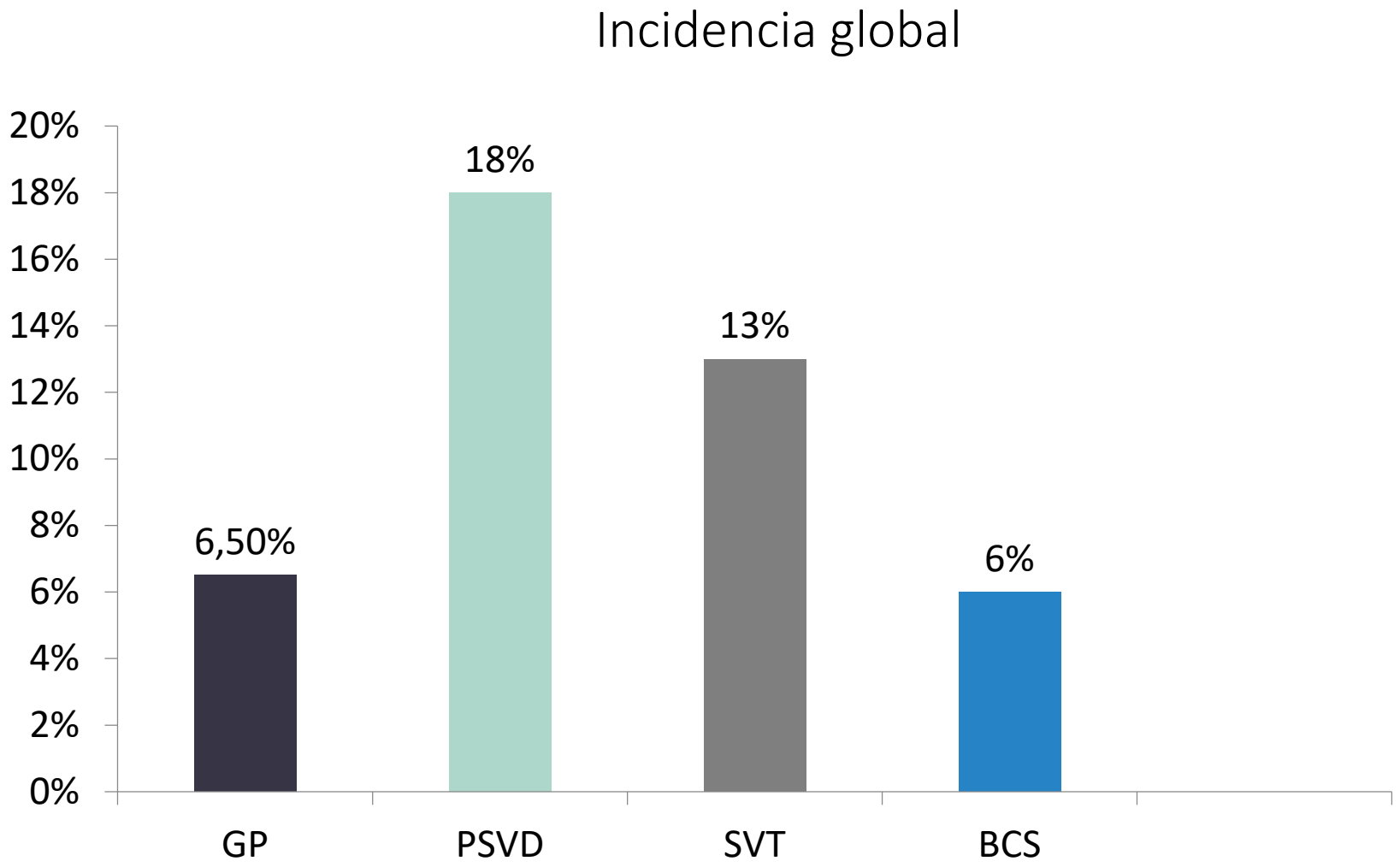
VALDIG
VASCULAR LIVER DISEASE GROUP

REHEVASC



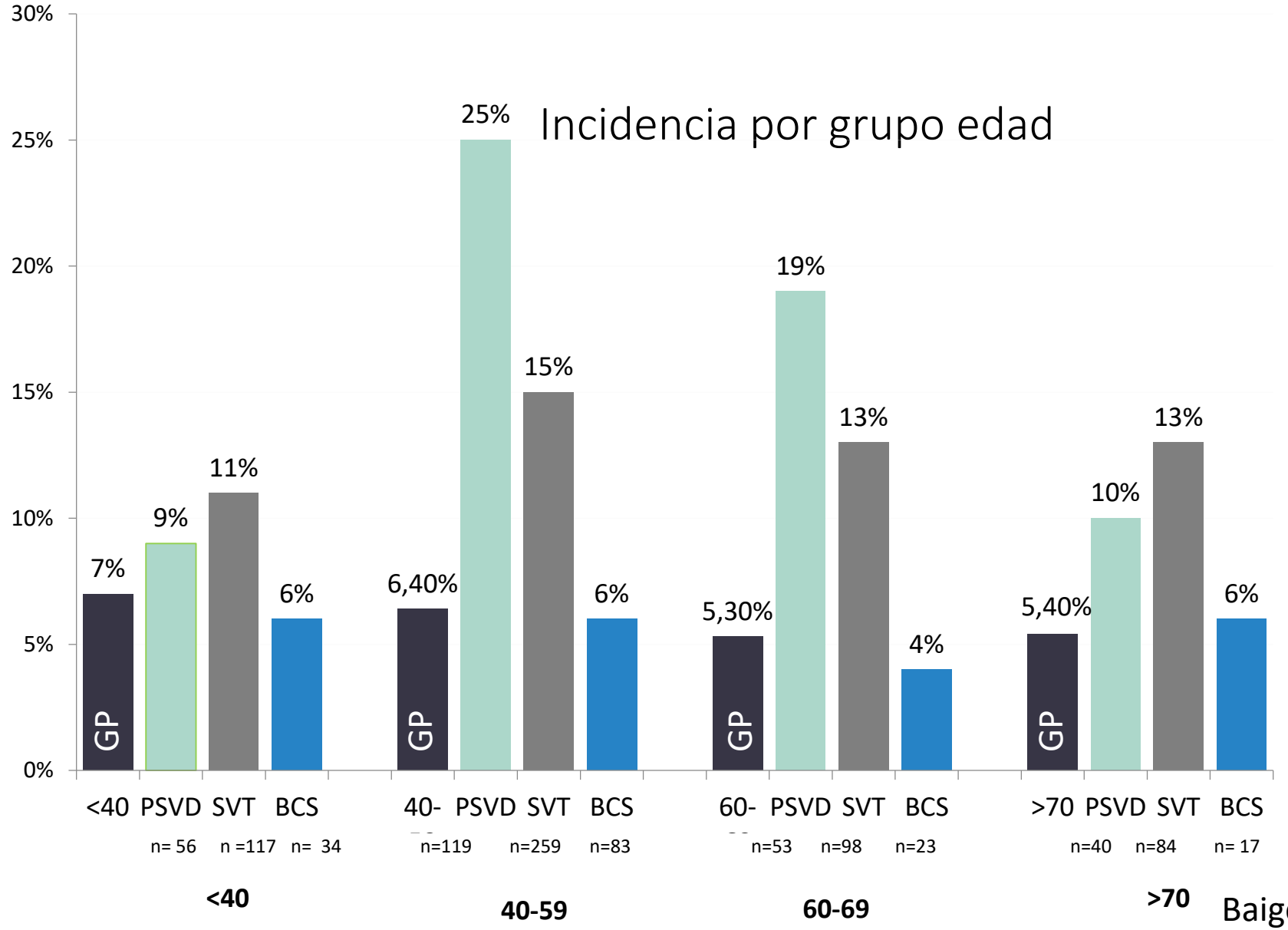

Baiges A et al. Unpublished

# Infección por SARS-CoV2 & Enfermedad Vascular Hepática




Baiges A et al. Unpublished

# Infección por SARS-CoV2 & Enfermedad Vascular Hepática




Baiges A et al. Unpublished

# Infección por SARS-CoV2 & Enfermedad Vascular Hepática

| | N (%) | Admission | ICU | Mortality |
|---|---|---|---|---|
| General population | 3.042.127 (6.5%) | 221.118 (7.3%) | 20.362 (0.7%) | 45.797 (1.5%) |
| VLD | 129 (13%) | 19 (14.7%) | 4 (3%) | 5 (4%) |
| PSVD | 48 | 5 (10%) | 2 (4%) | 1 (2%) |
| BCS | 9 | 1 (11%) | 0 | 0 |
| SVT | 72 | 13 (18%) | 2 (3%) | 4 (5%) |

Baiges A et al. Unpublished

# Gracias

IDIBAPS
Institut D'Investigacions Biomèdiques August Pi i Sunyer

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Hepatological Diseases (ERN RARE-LIVER)

CLÍNIC BARCELONA
Hospital Universitari