

Anomalies hépatiques et COVID-19

Point au 27/03/2020

Anomalies hépatiques et COVID-19

Mineures et Occasionnelles

A la prise en charge initiale

- ALAT et ASAT parfois légèrement augmentées
 - 25%-35% des patients (extrêmes 4% - 50%)
 - médiane 23-39 U/L, IQR habituel 20-50 U/L
 - ALAT /ASAT = 1
- Bilirubine et INR normaux
- Albuminémie diminuée
- GGT et PAL peu perturbées (mal documentées)

Anomalies hépatiques et COVID-19

Parallèles à la sévérité

- ALAT et ASAT statistiquement plus élevées (à la prise en charge)
 - dans les formes symptomatiques
 - dans les formes sévères
 - dans les formes nécessitant des soins intensifs
 - chez les patients qui ne survivront pas
- Valeur pronostique par ordre décroissant
 - Albuminémie >> ASAT >> bilirubinémie >> ALAT

Indicateurs initiaux d'admission en Unité de S.I.

| | Univariate logistic regression | | | Multivariate logistic regression | | |
|---|--------------------------------|------------|---------|----------------------------------|------------------|--------------|
| | OR | 95% CI | P value | OR | 95% CI | P value |
| Age | 1.08 | 1.04–1.13 | <0.001 | 1.06 | 1.00–1.12 | 0.046 |
| Male | 7.10 | 2.04–24.07 | 0.002 | 3.38 | 0.77–14.9 | 0.11 |
| Comorbidity | 4.34 | 1.70–11.10 | 0.002 | 1.83 | 0.50–6.75 | 0.36 |
| Fever | 1.52 | 0.34–6.85 | 0.14 | | | |
| White blood cells ($\times 10^9$ per L) | 1.28 | 1.08–1.52 | 0.004 | 1.07 | 0.79–1.45 | 0.66 |
| Lymphocytes ($\times 10^9$ per L) | 0.24 | 0.08–0.75 | 0.01 | 4.05 | 0.89–18.5 | 0.07 |
| C-reactive protein (mg/L) | 1.04 | 1.02–1.05 | <0.001 | 1.01 | 0.99–1.03 | 0.58 |
| Erythrocyte sedimentation rate (mm/h) | 1.00 | 0.99–1.02 | 0.58 | | | |
| Albumin (g/L) | 0.75 | 0.66–0.85 | <0.001 | 0.95 | 0.78–1.16 | 0.60 |
| Alanine aminotransferase (U/L) | 1.01 | 1.0–1.03 | 0.15 | | | |
| Aspartate aminotransferase (U/L) | 1.02 | 1.0–1.03 | 0.05 | 0.99 | 0.96–1.03 | 0.86 |
| Albumin (g/L) | 0.75 | 0.66–0.85 | <0.001 | 0.95 | 0.78–1.16 | 0.60 |
| Lactate dehydrogenase (U/L) | 1.01 | 1.0–1.02 | <0.001 | 1.01 | 1.0–1.02 | 0.08 |
| Lactate (mmol/L) | 1.23 | 0.88–1.70 | 0.22 | | | |
| Estimated glomerular filtration rate (mL/min/1.73m ²) | 0.98 | 0.96–0.99 | <0.001 | 0.99 | 0.89–1.02 | 0.89 |
| CD4 T cell counts (Per 100 cells/uL) | 0.45 | 0.31–0.64 | <0.001 | 0.55 | 0.33–0.92 | 0.02 |
| Radiological lesion | 4.46 | 0.62–31.9 | 0.14 | | | |

CI: Confidential interval, OR: Odds ratio.

Indicateurs initiaux de risque de décès

| | Total (n=191) | Non-survivor (n=54) | Survivor (n=137) | p value |
|--|-------------------------|--------------------------|------------------------|----------|
| (Continued from previous page) | | | | |
| Anaemia | 29 (15%) | 14 (26%) | 15 (11%) | 0.0094 |
| Platelet count, $\times 10^9$ per L | 206.0 (155.0-262.0) | 165.5 (107.0-229.0) | 220.0 (168.0-271.0) | <0.0001 |
| <100 | 13 (7%) | 11 (20%) | 2 (1%) | <0.0001 |
| Albumin, g/L | 32.3 (29.1-35.8) | 29.1 (26.5-31.3) | 33.6 (30.6-36.4) | <0.0001 |
| ALT, U/L | 30.0 (17.0-46.0) | 40.0 (24.0-51.0) | 27.0 (15.0-40.0) | 0.0050 |
| >40 | 59/189 (31%) | 26 (48%) | 33/135 (24%) | 0.0015 |
| Creatinine >133 μ mol/L | 8/186 (4%) | 5 (9%) | 3/132 (2%) | 0.045 |
| Lactate dehydrogenase, U/L | 300.0 (234.0-407.0) | 521.0 (363.0-669.0) | 253.5 (219.0-318.0) | <0.0001 |
| >245 | 123/184 (67%) | 53 (98%) | 70/130 (54%) | <0.0001 |
| Creatine kinase, U/L | 21.5 (13.0-72.4) | 39.0 (19.5-151.0) | 18.0 (12.5-52.1) | 0.0010 |
| >185 | 22/168 (13%) | 11/52 (21%) | 11/116 (9%) | 0.038 |
| High-sensitivity cardiac troponin I, pg/mL | 4.1 (2.0-14.1) | 22.2 (5.6-83.1) | 3.0 (1.1-5.5) | <0.0001 |
| >28 | 24/145 (17%) | 23/50 (46%) | 1/95 (1%) | <0.0001 |
| Prothrombin time, s | 11.6 (10.6-13.0) | 12.1 (11.2-13.7) | 11.4 (10.4-12.6) | 0.0004 |
| <16 | 171/182 (94%) | 47 (87%) | 124/128 (97%) | 0.016 |
| ≥ 16 | 11/182 (6%) | 7 (13%) | 4/128 (3%) | .. |
| D-dimer, μ g/mL | 0.8 (0.4-3.2) | 5.2 (1.5-21.1) | 0.6 (0.3-1.0) | <0.0001 |
| ≤ 0.5 | 55/172 (32%) | 4 (7%) | 51/118 (43%) | <0.0001* |
| >0.5 to ≤ 1 | 45/172 (26%) | 6 (11%) | 39/118 (33%) | .. |
| >1 | 72/172 (42%) | 44 (81%) | 28/118 (24%) | .. |
| Serum ferritin, μ g/L | 722.0 (377.2-1435.3) | 1435.3 (728.9-2000.0) | 503.2 (264.0-921.5) | <0.0001 |
| >300 | 102/128 (80%) | 44/46 (96%) | 58/82 (71%) | 0.0008 |
| IL-6, pg/mL | 7.4 (5.3-10.8) | 11.0 (7.5-14.4) | 6.3 (5.0-7.9) | <0.0001 |
| Procalcitonin, ng/mL | 0.1 (0.1-0.1) | 0.1 (0.1-0.5) | 0.1 (0.1-0.1) | <0.0001 |
| <0.1 | 114/164 (70%) | 19/51 (37%) | 95/113 (84%) | <0.0001* |
| ≥ 0.1 to <0.25 | 30/164 (18%) | 16/51 (31%) | 14/113 (12%) | .. |
| ≥ 0.25 to <0.5 | 6/164 (4%) | 3/51 (6%) | 3/113 (3%) | .. |
| ≥ 0.5 | 14/164 (9%) | 13/51 (25%) | 1/113 (1%) | .. |
| Imaging features | | | | |
| Consolidation | 112 (59%) | 40 (74%) | 72 (53%) | 0.0065 |
| Ground-glass opacity | 136 (71%) | 44 (81%) | 92 (67%) | 0.049 |
| Bilateral pulmonary infiltration | 143 (75%) | 45 (83%) | 98 (72%) | 0.090 |

Data are median (IQR), n (%), or n/N (%). p values were calculated by Mann-Whitney U test, χ^2 test, or Fisher's exact test, as appropriate. SOFA=Sequential Organ Failure Assessment. qSOFA=Quick SOFA. ALT=alanine aminotransferase. IL-6=interleukin-6. * χ^2 test comparing all subcategories.

Table 1: Demographic, clinical, laboratory, and radiographic findings of patients on admission

| | Univariable OR (95% CI) | p value | Multivariable OR (95% CI) | p value |
|---|----------------------------|---------|------------------------------|---------|
| Demographics and clinical characteristics | | | | |
| Age, years* | 1.14 (1.09-1.18) | <0.0001 | 1.10 (1.03-1.17) | 0.0043 |
| Female sex (vs male) | 0.61 (0.31-1.20) | 0.15 | .. | .. |
| Current smoker (vs non-smoker) | 2.23 (0.65-7.63) | 0.20 | .. | .. |
| Comorbidity present (vs not present) | | | | |
| Chronic obstructive lung disease | 5.40 (0.96-30.40) | 0.056 | .. | .. |
| Coronary heart disease | 21.40 (4.64-98.76) | <0.0001 | 2.14 (0.26-17.79) | 0.48 |
| Diabetes | 2.85 (1.35-6.05) | 0.0062 | .. | .. |
| Hypertension | 3.05 (1.57-5.92) | 0.0010 | .. | .. |
| Respiratory rate, breaths per min | | | | |
| ≤ 24 | 1 (ref) | .. | .. | .. |
| >24 | 8.89 (4.34-18.19) | <0.0001 | .. | .. |
| SOFA score | 6.14 (3.48-10.85) | <0.0001 | 5.65 (2.61-12.23) | <0.0001 |
| qSOFA score | 12.00 (5.06-28.43) | <0.0001 | .. | .. |
| Laboratory findings | | | | |
| White blood cell count, $\times 10^9$ per L | | | | |
| <4 | 0.73 (0.26-2.10) | 0.56 | .. | .. |
| 4-10 | 1 (ref) | .. | .. | .. |
| >10 | 6.60 (3.02-14.41) | <0.0001 | .. | .. |
| Lymphocyte count, $\times 10^9$ per L* | 0.02 (0.01-0.08) | <0.0001 | 0.19 (0.02-1.62) | 0.13 |
| ALT, U/L | .. | .. | .. | .. |
| ≤ 40 | 1 (ref) | .. | .. | .. |
| >40 | 2.87 (1.48-5.57) | 0.0018 | .. | .. |

(Table 3 continues in next column)

| | Univariable OR (95% CI) | p value | Multivariable OR (95% CI) | p value |
|---|----------------------------|---------|------------------------------|---------|
| (Continued from previous column) | | | | |
| Creatinine, μmol/L | | | | |
| ≤ 133 | 1 (ref) | .. | .. | .. |
| >133 | 4.39 (1.01-19.06) | 0.048 | .. | .. |
| Lactate dehydrogenase, U/L | | | | |
| ≤ 245 | 1 (ref) | .. | .. | .. |
| >245 | 45.43 (6.10-338.44) | 0.0002 | .. | .. |
| Creatine kinase, U/L | | | | |
| ≤ 185 | 1 (ref) | .. | .. | .. |
| >185 | 2.56 (1.03-6.36) | 0.043 | .. | .. |
| High-sensitivity cardiac troponin I, pg/mL | | | | |
| ≤ 28 | 1 (ref) | .. | .. | .. |
| >28 | 80.07 (10.34-620.36) | <0.0001 | .. | .. |
| D-dimer, μg/mL | | | | |
| ≤ 0.5 | 1 (ref) | .. | 1 (ref) | .. |
| >0.5 | 1.96 (0.52-7.43) | 0.32 | 2.14 (0.21-21.39) | 0.52 |
| >1 | 20.04 (6.52-61.56) | <0.0001 | 18.42 (2.64-128.55) | 0.0033 |
| Prothrombin time, s | | | | |
| <16 | 1 (ref) | .. | .. | .. |
| ≥ 16 | 4.62 (1.29-16.50) | 0.019 | .. | .. |
| Serum ferritin, μg/L | | | | |
| ≤ 300 | 1 (ref) | .. | .. | .. |
| >300 | 9.10 (2.04-40.58) | 0.0038 | .. | .. |
| IL-6, pg/mL* | 1.12 (1.03-1.23) | 0.0080 | .. | .. |
| Procalcitonin, ng/mL* | 13.75 (1.81-104.40) | 0.011 | .. | .. |

OR=odds ratio. SOFA=Sequential Organ Failure Assessment. qSOFA=Quick SOFA. ALT=alanine aminotransferase. IL-6=interleukin-6. *Per 1 unit increase.

Table 3: Risk factors associated with in-hospital death

hospitalised with COVID-19. In particular, older age

Anomalies hépatiques et COVID-19

Mécanisme incertain ce jour

- Données trop préliminaires sur la possibilité de trouver du virus dans le foie ou les voies biliaires
- Élément du syndrome de réaction inflammatoire
- Une augmentation marquée des tests hépatiques suggère d'abord une autre cause
 - Médicament (paracétamol, antibiotiques)
 - Hypoxie hépatique
 - Interaction
 - avec une maladie du foie sous jacente, connue ou non
 - avec une anomalie congénitale inapparente des transporteurs biliaires
- COVID-19 → myocardite (et rhabdomyolyse) → élévation des ASAT

Hypothétique

Raisonné

Pragmatique

Piège