## Supplemental information

# Body composition and short-term mortality in patients critically ill with acute-on-chronic liver failure

**Thomas Mangana del Rio, Sophie-Caroline Sacleux, Julien Vionnet, Philippe Ichaï, Alban Denys, Antoine Schneider, Audrey Coilly, Montserrat Fraga, Alexandre Wetzel, Joachim Koerfer, Jean-Daniel Chiche, Faouzi Saliba, Darius Moradpour, Fabio Becce, and Florent Artru**

**Supplementary materials**

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**Patients and Methods**

1. ICD-10 codes

The following ICD-10 codes were used to retrospectively screen for the presence of liver cirrhosis:
-   chronic liver disease: K70.0, K70.2, K73.X, K754, K758, K75.9, K76.0, B18.0, B18.1, B18.2, B18.8, B18.9
-   cirrhosis codes: K70.30, K70.31, K71.7, K72.1, K74.4, K74.5, K74.60, K74.69, K74.3, K72.1, K72.9
-   alcoholic liver disease: K70.4, K70.9
-   ascites and spontaneous bacterial peritonitis: R18.8, K70.31, K70.11 K65.2, K65.0, K65.9
-   varices: I85.9, I85.00, I86.4, I98.2, I85.10 I85.01, I98.3, I85.11
-   hepatic encephalopathy: K70.41, K72.11, K72.91, B15.0, B16.0, B16.2, 17.11, B19.0, B19.11, B19.21, G31.2, G93.4
-   portal hypertension and hepatorenal syndrome: K76.6, K76.7


2. Definition and site of infection

Diagnostic criteria for bacterial infections were the following:
-   spontaneous bacterial peritonitis: polymorphonuclear (PMN) cell count in ascitic fluid ≥ 250/mm3;
-   urinary tract infection: abnormal urinary sediment (> 10 leukocytes/field) and positive urinary culture;
-   bacteraemia: positive blood cultures;
-   pneumonia: clinical signs of infection and new infiltrates on chest x-ray;
-   skin and soft tissue infections: clinical signs of infection, swelling, erythema, heat and tenderness in the skin;
-   cholangitis: cholestasis, right upper quadrant pain and/or jaundice and radiological evidence for biliary obstruction;
-   secondary peritonitis: PMN count in ascitic fluid ≥ 250/mm³ and evidence (abdominal CT/surgery) of an intraabdominal source of infection;
-   *Clostridioides difficile* infection: positive stool toxin in a patient with diarrhea.
The other infections were diagnosed according to conventional criteria.

**Fig. S1. Flowchart of patient inclusion from the Lausanne cohort.** ACLF, acute-on-chronic liver failure; ICU, intensive care unit.
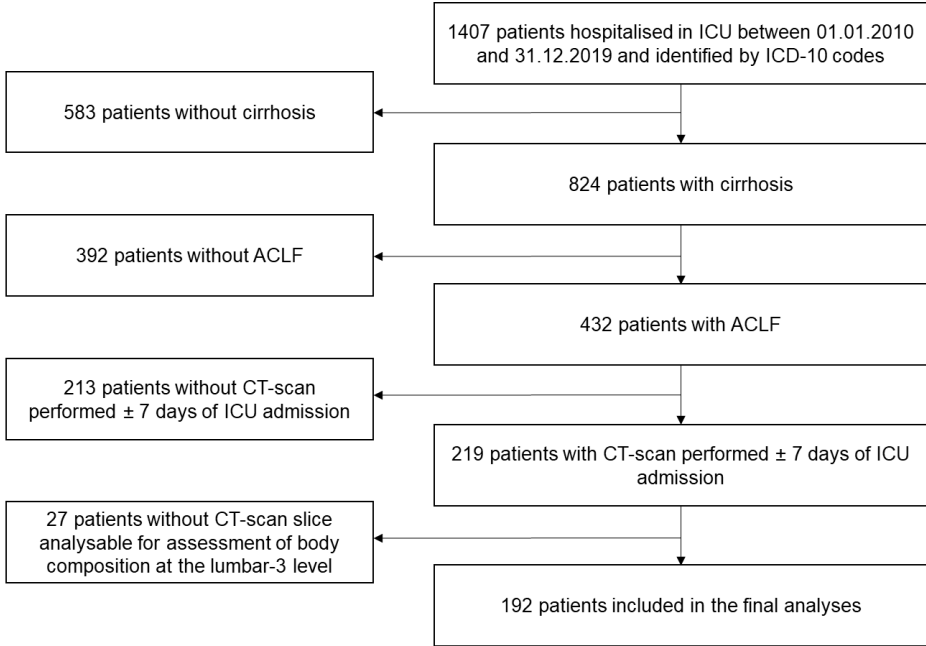


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**Fig. S2**. Performances of the available and newly developed models (Model d1 and d3) in male patients from the Lausanne cohort. (**A**) Receiver operating characteristic curves for survival at 28 days in the male patients' cohort as determined by the Model d1 (0.78 [0.68-0.85]) and Model d3 (0.90 [0.83-0.94]) *vs*. the CLIF-C ACLF-lactate score on day 1 (0.69 [0.59-0.78], p=0.002) and day 3 (0.86 [0.78-0.91], p=0.04). (**B**) Kaplan-Meier survival analysis of the male patients' cohort according to the Model d1 (cut-off ≤ 0.49). (**C**) Kaplan-Meier survival analysis of the male patients' cohort according to the Model d3 (cut-off ≤ 0.71).



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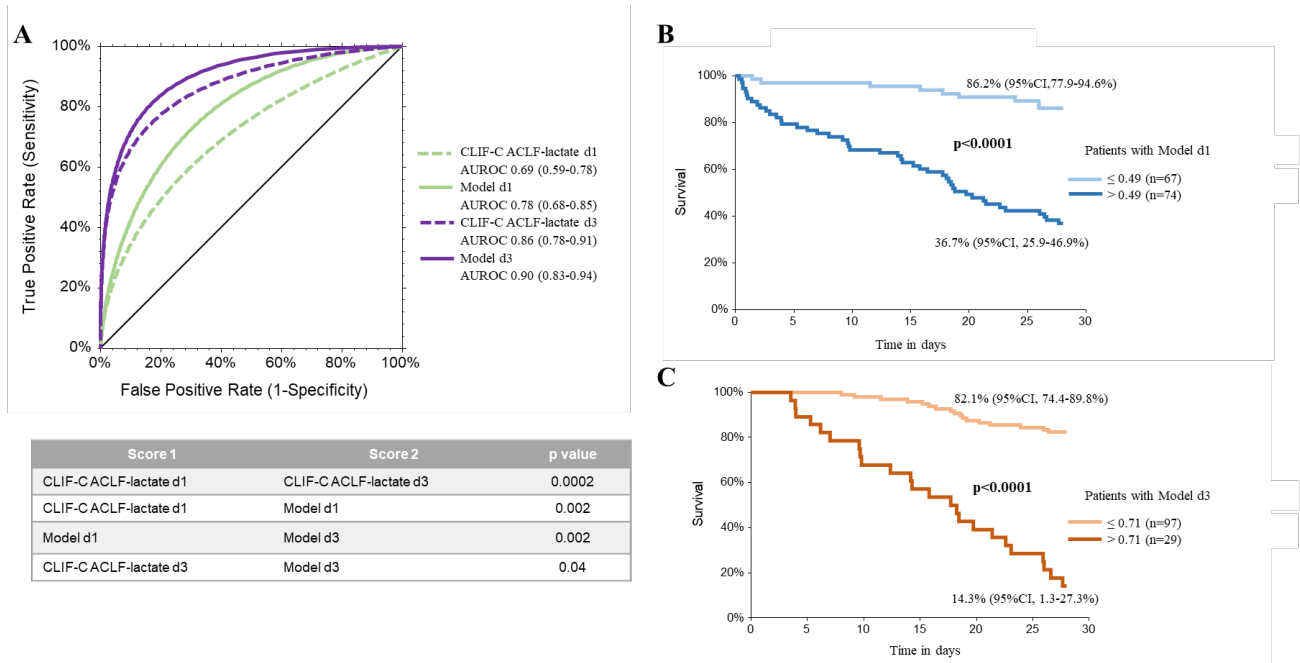
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**Fig. S3:** Performances of the available and newly developed models (Model d1 and d3) in female patients from the Lausanne cohort. **(A)** Receiver operating characteristic curves for survival at 28 days in female patients' cohort as determined by the Model d1 (0.91 [0.79-0.96]) and Model d3 (0.93 [0.81-0.97]) *vs.* the CLIF-C ACLF-lactate score on day 1 (0.90 [0.75-0.95], p=0.62) and day 3 (0.93 [0.81-0.98], p=0.91). **(B)** Kaplan-Meier survival analysis of the female patients' cohort according to the Model d1 (cut-off ≤ 0.49). **(C)** Kaplan-Meier survival analysis of the female patients' cohort according to the Model d3 (cut-off ≤ 0.71).



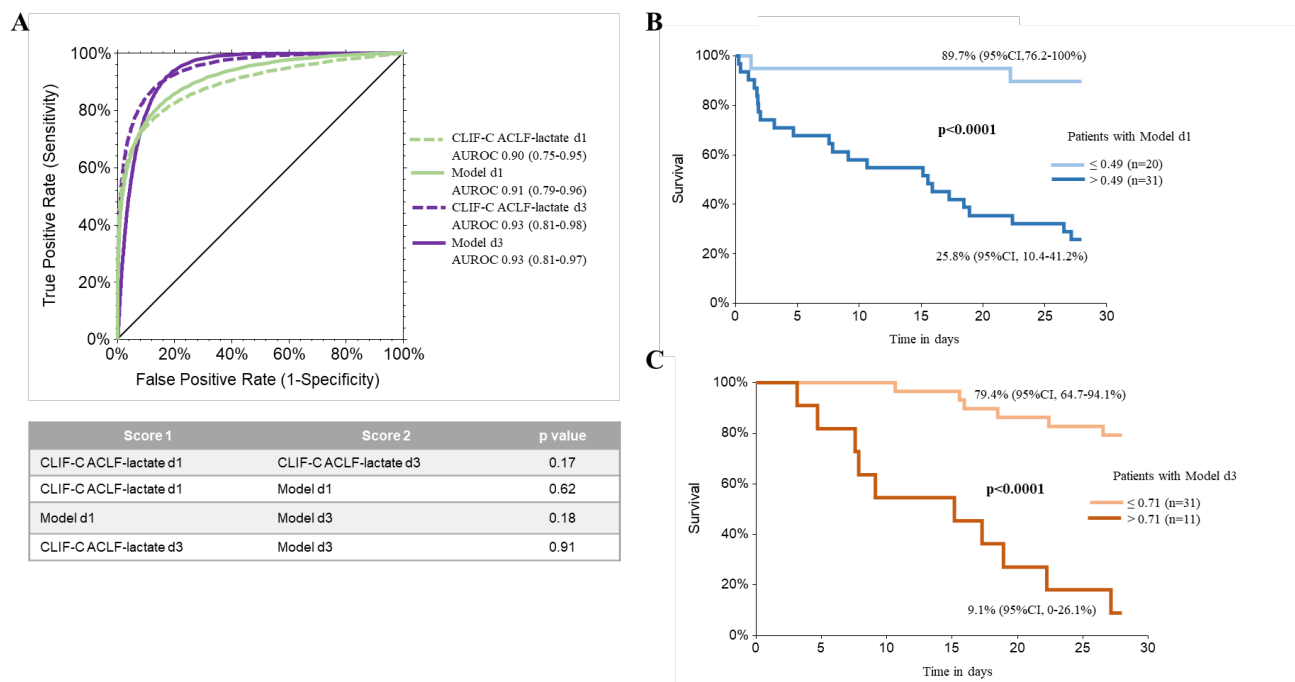| Score 1 | Score 2 | p value |
|---|---|---|
| CLIF-C ACLF-lactate d1 | CLIF-C ACLF-lactate d3 | 0.17 |
| CLIF-C ACLF-lactate d1 | Model d1 | 0.62 |
| Model d1 | Model d3 | 0.18 |
| CLIF-C ACLF-lactate d3 | Model d3 | 0.91 |

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Supplementary Figure 3

**Table S1:** Comparison of the main characteristics on day 1 between patients from Lausanne included in the final analyses (n=192) and patients with cirrhosis and ACLF not included in the final analyses (CT not performed or absence of CT-scan slice allowing for body composition evaluation) (n=240). Continuous and categorical variables are expressed respectively in median (interquartile range) and N (percentages). Comparisons were performed using the Student's t-test or Mann-Whitney U test for quantitative variables or Chi-Square and Fisher exact tests for categorical variables as appropriate

| | Overall population included in the final analyses (n=192) | Patients with cirrhosis and ACLF not included in the final analyses (CT not performed or absence of CT-scan slice allowing for body composition evaluation) (n=240)) | p |
|---|---|---|---|
| **Characteristics** | | | |
| Age (years) | 62.0 (53.2-70.0) | 63.0 (54.0-70.8) | 0.72 |
| Sex (male) | 141 (73.5) | 181 (76.7) | 0.45 |
| BMI (kg/m$^2$) | 25.8 (22.3-31.2) | 26.1 (22.7 – 28.8) | 0.36 |
| Ethnicity Caucasian Hispanic Other | 161 (83.8) 16 (8.3) 15 (7.8) | 178 (74.2) 34 (14.2) 28 (11.7) | 0.09 |
| **Aetiology** | | | |
| Alcohol Viral Metabolic Other | 129 (67.2) 34 (17.7) 18 (9.4) 11 (5.7) | 167 (70.7) 35 (14.8) 20 (8.5) 14 (6.0) | 0.96 |
| **Cause for ICU admission** | | | |
| Sepsis Bleeding Other | 79 (41.1) 63 (32.8) 50 (26.1) | 82 (34.2) 94 (39.1) 64 (26.7) | 0.22 |
| **Laboratory on day 1** | | | |
| Leukocytes (G/l) | 15.0 (10.1-20.8) | 13.6 (9.7-19.3) | 0.04 |
| INR | 1.5 (1.3-1.8) | 1.4 (1.2-1.7) | 0.07 |
| Bilirubin (mg/dl) | 5.3 (3.7-8.2) | 4.5 (3.3-6.6) | 0.32 |
| AST (IU) | 93.0 (48.0-299.5) | 80 (44.0-268.0) | 0.31 |
| Albumin (g/l) | 27.0 (23.2-31.0) | 28.0 (24.0-32.0) | 0.26 |
| Creatinine (mg/dl) | 1.4 (1.0-2.1) | 1.4 (0.8-2.3) | 0.28 |
| Sodium (mmol/l) | 138.0 (134.0-141.0) | 138.0 (134.0-141.0) | 0.83 |
| Lactate (mmol/l) | 4.1 (2.4-7.4) | 3.0 (2.0-5.4) | 0.21 |
| Ammonia, (µmol/l) | 71.0 (53.0-112.0) | 65.0 (45-101) | 0.47 |
| CRP (mg/l) | 55.0 (20.0-112.5) | 39.0 (13.0-92.0) | 0.02 |
| **ACLF grade on day 1** | | | |
| 0 1 2 3 | 0 (0) 26 (13.6) 59 (30.7) 107 (55.7) | 0 (0) 22 (9.1) 95 (39.6) 123 (51.3) | 0.09 |
| **Scores on day 1** | | | |
| MELD | 21.9 (15.1-27.9) | 19.1 (14.4-28.6) | 0.30 |
| CLIF-C ACLF | 67.5 (51.8-72.7) | 66.6 (61.5-72.1) | 0.64 |
| CLIF-C ACLF-lactate | 71.5 (64.1-80.2) | 69.5 (62.7-78.3) | 0.08 |

**Table S2:** Comparison of the main characteristics on day 1 between patients included in the final analyses (n=192) and patients with cirrhosis and without ACLF in whom a CT was performed at admission to the intensive care unit (ICU) ± 7 days (n=131). Continuous and

| | Overall population included in the final analyses (n=192) | Cirrhotic patients without ACLF who underwent a CT on admission ± 7 days (n=131) | p |
|---|---|---|---|
| **Characteristics** | | | |
| Age (years) | 62.0 (53.2-70.0) | 66.0 (50.0-75.0) | 0.89 |
| Sex (male) | 141 (73.5) | 93 (70.9) | 0.24 |
| BMI (kg/m$^2$) | 25.8 (22.3-31.2) | 25.4 (21.4 – 27.6) | 0.58 |
| Ethnicity Causasian Hispanic Other | 161 (83.8) 16 (8.3) 15 (7.8) | 102 (77.9) 13 (9.9) 14 (10.7) | 0.18 |
| Clinical frailty scale (score) | 4.0 (3.0-4.0) | 3.0 (2.0-4.0) | 0.02 |
| **Aetiology** | | | |
| Alcohol Viral Metabolic Other | 129 (67.2) 34 (17.7) 18 (9.4) 11 (5.7) | 99 (75.6) 6 (4.5) 20 (15.4) 6 (4.5) | 0.007 |
| **Cause for ICU admission** | | | |
| Sepsis Bleeding Other | 79 (41.1) 63 (32.8) 50 (26.1) | 10 (7.6) 58 (44.3) 63 (48.1) | <0.0001 |
| **Laboratory on day 1** | | | |
| Leukocytes (G/l) | 15.0 (10.1-20.8) | 11.6 (7.2-16.7) | 0.03 |
| INR | 1.5 (1.3-1.8) | 1.3 (1.1-1.6) | 0.009 |
| Bilirubin (mg/dl) | 5.3 (3.7-8.2) | 4.2 (3.3-5.6) | 0.001 |
| AST (IU) | 93.0 (48.0-299.5) | 73 (34.0-168.0) | 0.07 |
| Albumin (g/l) | 27.0 (23.2-31.0) | 32.0 (27.0-38.0) | 0.007 |
| Creatinine (mg/dl) | 1.4 (1.0-2.1) | 1.1 (0.7-1.9) | 0.03 |
| Sodium (mmol/l) | 138.0 (134.0-141.0) | 138.0 (134.0-142.0) | 0.93 |
| Lactate (mmol/l) | 4.1 (2.4-7.4) | 2.4 (1.3-3.8) | 0.21 |
| Ammonia, (µmol/l) | 71.0 (53.0-112.0) | 61.0 (41-92) | 0.47 |
| CRP (mg/l) | 55.0 (20.0-112.5) | 45.0 (18.0-98.0) | 0.07 |
| **ACLF grade on day 1** | | | |
| 0 1 2 3 | 0 (0) 26 (13.6) 59 (30.7) 107 (55.7) | 131 (100) 0 (0) 0 (0) 0 (0) | <0.0001 |
| **Scores on day 1** | | | |
| MELD | 21.9 (15.1-27.9) | 16.1 (12.4-21.6) | <0.0001 |
| CLIF-C ACLF | 67.5 (51.8-72.7) | 46.8 (41.4-51.1) | <0.0001 |
| CLIF-C ACLF-lactate | 71.5 (64.1-80.2) | 47.1 (42.1-52.3) | <0.0001 |
| **Outcome** | | | |
| 28-day survival, % (95%CI) | 58.2 (51.2-65.2) | 94.5 (90.1-98.5) | <0.0001 |
| **Body composition parameters** | | | |
| L3SMI (cm$^2$/m$^2$) | 43.2 (37.1-50.1) | 46.8 (36.3-57.8) | 0.009 |
| Sarcopenia according to L3SMI sex specific cut-offs | 121 (63.0) | 61 (46.5) | 0.01 |
| SMRA (HU) | 36.0 (31.0-41.0) | 39.9 (28.6-47.2) | 0.08 |
| IMATI (cm$^2$/m$^2$) | 6.3 (3.9-10.0) | 4.9 (2.8-7.9) | 0.01 |
| VATI (cm$^2$/m$^2$) | 44.3 (24.4-69.9) | 49.4 (22.6-87.1) | 0.03 |
| SATI (cm$^2$/m$^2$) | 48.6 (27.0-70.3) | 53.0 (31.1-78.9) | 0.01 |
| VSR | 0.9 (0.6-1.4) | 0.9 (0.6-1.8) | 0.18 |
| VAT-RA (HU) | -81.2 (-88.5 to -75.8) | -84.5 (-92.8 to -78.8) | 0.002 |
| SAT-RA (HU) | -86.6 (-95.7 to -76.8) | -88.3 (-100.1 to -75.2) | 0.02 |

categorical variables are expressed in median (interquartile range) and N (percentages), respectively. Comparisons were performed using the Student's t-test or Mann-Whitney U test for quantitative variables or Chi-Square and Fisher exact tests for categorical variables as appropriate

**Table S3**: Univariable and multivariable analyses of predictors of 28-days mortality in male patients from Lausanne cohort on day 1 (n=141)

| Covariant | Univariable analysis | | | Multivariable analysis | | |
|---|---|---|---|---|---|---|
| | OR | 95% CI | p value | OR | 95% CI | p value |
| **Characteristics** | | | | | | |
| Age (years) | 0.99 | 0.96-1.02 | 0.6 | | | |
| Sex (male) | - | - | - | | | |
| BMI (kg/m$^2$) | 1.03 | 0.96-1.10 | 0.4 | | | |
| Ethnicity | | | | | | |
| Caucasian | - | - | - | | | |
| Hispanic | 2.42 | 0.82-5.03 | 0.15 | | | |
| Other | 0.81 | 0.11-6.21 | 0.45 | | | |
| Clinical frailty scale (score) | 1.05 | 0.81-1.92 | 0.22 | | | |
| **Aetiology** | | | | | | |
| Alcohol | - | - | - | - | - | - |
| Viral | 2.26 | 0.98-5.23 | 0.06 | 2.09 | 0.71-6.13 | 0.17 |
| Metabolic | 0.57 | 0.14-2.28 | 0.43 | 0.54 | 0.09-3.07 | 0.48 |
| Other | 0.34 | 0.04-3.09 | 0.34 | 0.29 | 0.03-3.02 | 0.30 |
| **Cause for ICU admission** | | | | | | |
| Sepsis | - | - | - | - | - | - |
| Bleeding | 0.43 | 0.19-0.95 | 0.04 | 0.79 | 0.28-2.16 | 0.64 |
| Other | 0.59 | 0.23-1.49 | 0.26 | 0.81 | 0.22-2.95 | 0.75 |
| **Laboratory** | | | | | | |
| Leukocytes (G/l) | 1.00 | 0.96-1.03 | 0.91 | | | |
| INR | 3.23 | 1.61-6.49 | 0.0009 | | | |
| Bilirubin (mg/dl) | 1.11 | 1.04-1.20 | 0.002 | | | |
| AST (IU) | 1.00 | 0.99-1.01 | 0.11 | | | |
| Albumin (g/l) | 0.98 | 0.89-1.02 | 0.24 | | | |
| Creatinine (mg/dl) | 1.46 | 1.05-2.04 | 0.02 | | | |
| Sodium (mmol/l) | 0.98 | 0.93-1.03 | 0.62 | | | |
| Lactate (mmol/l) | 1.15 | 1.08-1.24 | 0.0006 | | | |
| Ammonia, (µmol/l) | 1.00 | 0.99-1.01 | 0.67 | | | |
| CRP (mg/l) | 0.99 | 0.99-1.01 | 0.55 | | | |
| **Organ failure** | | | | | | |
| Liver | 5.01 | 1.67-15.01 | 0.003 | | | |
| Kidney | 2.22 | 1.08-4.60 | 0.02 | | | |
| Brain | 1.06 | 0.92-1.89 | 0.16 | | | |
| Coagulation | 5.24 | 2.10-14.28 | 0.0005 | | | |
| Circulation | 4.71 | 1.03-21.80 | 0.02 | | | |
| Lungs | 1.63 | 1.03-3.22 | 0.02 | | | |
| **Organ support** | | | | | | |
| RRT | 2.20 | 1.10-6.33 | 0.02 | | | |
| Vasopressors | 4.71 | 1.03-21.80 | 0.02 | | | |
| Mechanical ventilation | 4.11 | 1.33-12.75 | 0.01 | | | |
| **Scores** | | | | | | |
| MELD | 1.08 | 1.04-1.13 | <0.0001 | | | |
| ACLF grade | 3.43 | 1.85-6.34 | <0.0001 | | | |
| CLIF-C ACLF | 1.07 | 1.03-1.12 | 0.001 | | | |
| CLIF-C ACLF lactate | 1.09 | 1.04-1.14 | <0.0001 | 1.08 | 1.03-1.13 | 0.0003 |
| **Body composition parameters** | | | | | | |
| L3SMI (cm$^2$/m$^2$)* | 0.95 | 0.91-0.98 | 0.03 | 0.97 | 0.94-1.01 | 0.07 |
| Sarcopenia (L3SMI cut-offs)* | 3.91 | 1.74-8.75 | 0.0009 | 3.21 | 1.13-9.05 | 0.03 |
| SMRA (HU) | 0.98 | 0.93-1.03 | 0.50 | | | |
| IMATI (cm$^2$/m$^2$) | 0.97 | 0.91-1.03 | 0.37 | | | |
| VATI (cm$^2$/m$^2$) | 0.99 | 0.98-1.01 | 0.35 | | | |
| SATI (cm$^2$/m$^2$) | 1.00 | 0.99-1.01 | 0.40 | | | |
| VSR | 0.61 | 0.33-1.26 | 0.21 | | | |
| VAT-RA (HU) ¶ | 1.04 | 1.01-1.09 | 0.05 | 1.03 | 0.97-1.09 | 0.24 |
| SAT-RA (HU) ¶ | 1.02 | 0.99-1.05 | 0.09 | 1.02 | 0.98-1.05 | 0.27 |
| SAT-RA (HU), according to (27) | 1.42 | 0.53-3.81 | 0.48 | | | |

*Not included in the multivariable analysis to avoid collinearity with sarcopenia according to L3SMI sex specific cut-offs.

¶ Not included in the multivariable analysis to collinearity (Spearman: 0.78 DF 102, p<0.0001).

**Table S4**: Univariable and multivariable analyses of predictors of 28-days mortality female patients from Lausanne cohort on day 1 (n=51)

| Covariant | Univariable analysis | | | Multivariable analysis | | |
|---|---|---|---|---|---|---|
| | OR | 95% CI | p value | OR | 95% CI | p value |
| **Characteristics** | | | | | | |
| Age (years) | 1.03 | 0.98-1.08 | 0.6 | | | |
| Sex (male) | - | - | - | | | |
| BMI (kg/m$^2$) | 1.00 | 0.89-1.12 | 0.9 | | | |
| Ethnicity | | | | | | |
| Caucasian | - | - | - | | | |
| Hispanic | 4.58 | 0.27-9.33 | 0.23 | | | |
| Other | 0.89 | 0.21-8.12 | 0.67 | | | |
| Clinical frailty score | 1.08 | 0.63-2.20 | 0.61 | | | |
| **Aetiology** | | | | | | |
| Alcohol | - | - | - | | | |
| Viral | 1.11 | 0.14-8.22 | 0.91 | | | |
| Metabolic | 1.11 | 0.19-6.290 | 0.89 | | | |
| Other | 1.67 | 0.24-11.26 | 0.59 | | | |
| **Cause for ICU admission** | | | | | | |
| Sepsis | - | - | - | | | |
| Bleeding | 0.76 | 0.16-3.33 | 0.70 | | | |
| Other | 0.82 | 0.24-2.83 | 0.75 | | | |
| **Laboratory** | | | | | | |
| Leukocytes (G/l) | 1.09 | 1.04-1.14 | <0.0001 | | | |
| INR | 5.97 | 2.84-12.54 | <0.0001 | | | |
| Bilirubin (mg/dl) | 1.08 | 1.03-1.13 | 0.0004 | | | |
| AST (IU) | 1.00 | 0.99-1.01 | 0.31 | | | |
| Albumin (g/l) | 1.07 | 1.00-1.15 | 0.03 | | | |
| Creatinine (mg/dl) | 1.16 | 0.70-1.95 | 0.55 | | | |
| Sodium (mmol/l) | 1.01 | 0.93-1.10 | 0.72 | | | |
| Lactate (mmol/l) | 1.16 | 1.02-1.32 | 0.02 | | | |
| Ammonia, (µmol/l) | 1.00 | 0.99-1.01 | 0.32 | | | |
| CRP (mg/l) | 1.00 | 0.99-1.01 | 0.89 | | | |
| **Organ failure** | | | | | | |
| Liver | 2.28 | 1.02-13.76 | 0.04 | | | |
| Kidney | 1.76 | 0.87-5.57 | 0.09 | | | |
| Brain | 1.05 | 0.76-3.61 | 0.23 | | | |
| Coagulation | 1.64 | 1.03-6.04 | 0.03 | | | |
| Circulation | 4.23 | 0.78-22.84 | 0.09 | | | |
| Lungs | 4.78 | 1.46-15.60 | 0.009 | | | |
| **Organ support** | | | | | | |
| RRT | 3.78 | 1.02-20.94 | 0.03 | | | |
| Vasopressors | 4.23 | 0.78-22.84 | 0.09 | | | |
| Mechanical ventilation | 10.66 | 1.22-93.12 | 0.03 | | | |
| **Scores** | | | | | | |
| MELD | 1.09 | 1.01-1.18 | 0.04 | | | |
| ACLF grade | 11.69 | 2.92-46.85 | 0.0005 | | | |
| CLIF-C ACLF | 1.26 | 1.11-1.50 | 0.0006 | | | |
| CLIF-C ACLF lactate | 1.26 | 1.11-1.43 | 0.0004 | 1.26 | 1.11-1.43 | 0.0004 |
| **Body composition parameters** | | | | | | |
| L3SMI (cm$^2$/m$^2$) | 3.41 | 0.23-48.97 | 0.40 | | | |
| Sarcopenia (L3SMI cut-offs) | 2.47 | 0.79-7.75 | 0.11 | | | |
| SMRA (HU) | 0.99 | 0.91-1.08 | 0.85 | | | |
| IMATI (cm$^2$/m$^2$) | 0.99 | 0.91-1.03 | 0.91 | | | |
| VATI (cm$^2$/m$^2$) | 1.00 | 0.98-1.03 | 0.54 | | | |
| SATI (cm$^2$/m$^2$) | 1.00 | 0.98-1.01 | 0.76 | | | |
| VSR | 1.56 | 0.62-4.68 | 0.45 | | | |
| VAT-RA (HU) | 1.03 | 0.98-1.10 | 0.18 | | | |
| SAT-RA (HU) | 1.04 | 1.01-1.08 | 0.05 | 1.01 | 0.98-1.07 | 0.18 |
| SAT-RA (HU), according to (27) | 1.71 | 0.46-6.39 | 0.42 | | | |

**Table S5:** Univariable and multivariable analyses of predictors of 28-days mortality in male patients from Lausanne cohort on day 3 (n=126)

| Covariant | Univariable analysis | | | Multivariable analysis | | |
|---|---|---|---|---|---|---|
| | OR | 95% CI | p value | OR | 95% CI | p value |
| **Characteristics** | | | | | | |
| Age (years) | 0.99 | 0.95-1.02 | 0.61 | | | |
| Sex (male) | - | - | - | | | |
| BMI (kg/m$^2$) | 1.01 | 0.93-1.09 | 0.77 | | | |
| Ethnicity | | | | | | |
| Caucasian | - | - | - | | | |
| Hispanic | 1.98 | 0.67-3.98 | 0.19 | | | |
| Other | 0.87 | 0.19-7.12 | 0.49 | | | |
| Clinical frailty score (score) | 1.15 | 0.87-1.89) | 0.12 | | | |
| **Aetiology** | | | | | | |
| Alcohol | - | - | - | - | - | - |
| Viral | 2.76 | 1.12-6.76 | 0.03 | 2.51 | 0.79-7.97 | 0.11 |
| Metabolic | 0.85 | 0.21-3.44 | 0.82 | 2.50 | 0.55-11.28 | 0.23 |
| Other | 0.64 | 0.06-6.04 | 0.70 | 0.16 | 0.01-2.65 | 0.20 |
| **Cause for ICU admission** | | | | | | |
| Sepsis | - | - | - | - | - | - |
| Bleeding | 0.43 | 0.18-1.03 | 0.06 | 0.48 | 0.15-1.56 | 0.22 |
| Other | 0.59 | 0.23-1.49 | 0.26 | 0.51 | 0.12-2.07 | 0.35 |
| **Laboratory** | | | | | | |
| Leukocytes (G/l) | 1.00 | 0.96-1.04 | 0.90 | | | |
| INR | 8.71 | 1.20-63.10 | 0.03 | | | |
| Bilirubin (mg/dl) | 1.11 | 1.01-1.23 | 0.02 | | | |
| AST (IU) | 1.00 | 0.99-1.01 | 0.68 | | | |
| Albumin (g/l) | 1.06 | 0.98-1.16 | 0.12 | | | |
| Creatinine (mg/dl) | 1.45 | 1.04-2.02 | 0.02 | | | |
| Sodium (mmol/l) | 0.99 | 0.94-1.06 | 0.97 | | | |
| Lactate (mmol/l) | 1.55 | 1.20-2.01 | 0.0009 | | | |
| Ammonia, (µmol/l) | 1.00 | 0.99-1.01 | 0.85 | | | |
| CRP (mg/l) | 0.99 | 0.99-1.01 | 0.86 | | | |
| **Organ failure** | | | | | | |
| Liver | 2.94 | 1.18-7.37 | 0.02 | | | |
| Kidney | 2.35 | 1.01-5.63 | 0.01 | | | |
| Brain | 1.68 | 0.87-6.64 | 0.12 | | | |
| Coagulation | 7.81 | 2.72-22.37 | 0.0002 | | | |
| Circulation | 4.20 | 1.88-9.41 | 0.0005 | | | |
| Lungs | 3.20 | 1.55-6.60 | 0.009 | | | |
| **Organ support** | | | | | | |
| RRT | 4.82 | 1.63-14.21 | 0.005 | | | |
| Vasopressors | 4.20 | 1.88-9.41 | 0.0005 | | | |
| Mechanical ventilation | 2.36 | 1.15-5.23 | 0.02 | | | |
| **Scores** | | | | | | |
| MELD | 1.13 | 1.07-1.20 | <0.0001 | | | |
| ACLF grade | 3.10 | 1.90-5.02 | <0.0001 | | | |
| CLIF-C ACLF | 1.17 | 1.10-1.25 | <0.0001 | | | |
| CLIF-C ACLF lactate | 1.18 | 1.11-1.27 | <0.0001 | 1.18 | 1.13-1.27 | <0.0001 |
| **Body composition parameters** | | | | | | |
| L3SMI (cm$^2$/m$^2$)* | 0.97 | 0.93-0.99 | 0.04 | 0.98 | 0.93-1.01 | 0.07 |
| Sarcopenia (L3SMI cut-offs)* | 4.11 | 1.64-10.31 | 0.002 | 1.95 | 0.95-6.79 | 0.06 |
| SMRA (HU) | 0.99 | 0.94-1.04 | 0.79 | | | |
| IMATI (cm$^2$/m$^2$) | 0.96 | 0.89-1.03 | 0.33 | | | |
| VATI (cm$^2$/m$^2$) | 0.98 | 0.97-1.01 | 0.13 | | | |
| SATI (cm$^2$/m$^2$) | 1.00 | 0.98-1.01 | 0.84 | | | |
| VSR | 0.75 | 0.36-1.52 | 0.42 | | | |
| VAT-RA (HU) ¶ | 1.06 | 1.01-1.13 | 0.02 | 1.04 | 0.95-1.12 | 0.23 |
| SAT-RA (HU) ¶ | 1.02 | 0.99-1.05 | 0.09 | 1.03 | 0.98-1.08 | 0.18 |
| SAT-RA (HU), according to (27) | 1.76 | 0.62-4.92 | 0.28 | | | |

*Not included in the same multivariable analysis to avoid collinearity

¶ Not included in the same multivariable analysis due to collinearity (Spearman: 0.79 DF 91, p<0.0001)

**Table S6**: Univariable and multivariable analyses of predictors of 28-day mortality in female patients from Lausanne cohort on day 3 (n=42)

| Covariant | Univariable analysis | | | Multivariable analysis | | |
|---|---|---|---|---|---|---|
| | OR | 95% CI | p value | OR | 95% CI | p value |
| **Characteristics** | | | | | | |
| Age (years) | 1.03 | 0.97-1.08 | 0.25 | | | |
| Sex (male) | - | - | - | | | |
| BMI (kg/m$^2$) | 0.97 | 0.85-1.12 | 0.75 | | | |
| Ethnicity | | | | | | |
| Caucasian | - | - | - | | | |
| Hispanic | 1.91 | 0.21-10.41 | 0.23 | | | |
| Other | 0.98 | 0.18-7.93 | 0.71 | | | |
| Clinical frailty scale (score) | 1.11 | 0.81-2.23 | 0.17 | | | |
| **Aetiology** | | | | | | |
| Alcohol | - | - | - | | | |
| Viral | 1.11 | 0.14-8.22 | 0.91 | | | |
| Metabolic | 1.11 | 0.19-6.290 | 0.89 | | | |
| Other | 1.67 | 0.24-11.26 | 0.59 | | | |
| **Cause for ICU admission** | | | | | | |
| Sepsis | - | - | - | | | |
| Bleeding | 0.64 | 0.11-3.50 | 0.61 | | | |
| Other | 0.70 | 0.17-2.84 | 0.62 | | | |
| **Laboratory** | | | | | | |
| Leukocytes (G/l) | 1.07 | 0.96-1.20 | 0.19 | | | |
| INR | 1.49 | 0.74-3.00 | 0.18 | | | |
| Bilirubin (mg/dl) | 1.07 | 1.01-1.20 | 0.04 | | | |
| AST (IU) | 1.00 | 0.99-1.01 | 0.16 | | | |
| Albumin (g/l) | 1.12 | 0.98-1.27 | 0.09 | | | |
| Creatinine (mg/dl) | 1.21 | 0.70-2.08 | 0.47 | | | |
| Sodium (mmol/l) | 1.00 | 0.91-1.11 | 0.91 | | | |
| Lactate (mmol/l) | 1.37 | 1.01-2.01 | 0.03 | | | |
| Ammonia, (µmol/l) | 1.00 | 0.99-1.01 | 0.29 | | | |
| CRP (mg/l) | 1.00 | 0.99-1.01 | 0.62 | | | |
| **Organ failure** | | | | | | |
| Liver | 6.89 | 1.18-40.27 | 0.03 | | | |
| Kidney | 2.50 | 0.85-11.21 | 0.08 | | | |
| Brain | 1.26 | 0.85-4.21 | 0.20 | | | |
| Coagulation | 11.36 | 1.18-109.02 | 0.02 | | | |
| Circulation | 1.94 | 1.02-6.94 | 0.03 | | | |
| Lungs | 2.22 | 1.13-4.38 | 0.03 | | | |
| **Organ support** | | | | | | |
| RRT | 5.73 | 1.21-61.12 | 0.02 | | | |
| Vasopressors | 1.94 | 1.02-6.94 | 0.03 | | | |
| Mechanical ventilation | 12.85 | 1.47-112.17 | 0.02 | | | |
| **Scores** | | | | | | |
| MELD | 1.10 | 1.02-1.19 | 0.01 | | | |
| ACLF grade | 2.42 | 1.15-5.12 | 0.009 | | | |
| CLIF-C ACLF | 1.21 | 1.06-1.37 | 0.002 | | | |
| CLIF-C ACLF lactate | 1.21 | 1.06-1.37 | 0.002 | 1.17 | 1.05-1.32 | 0.004 |
| **Body composition parameters** | | | | | | |
| L3SMI (cm$^2$/m$^2$)* | 2.60 | 0.16-45.11 | 0.50 | | | |
| Sarcopenia (L3SMI cut-offs) | 2.56 | 0.69-9.49 | 0.13 | | | |
| SMRA (HU) | 1.03 | 0.93-1.14 | 0.52 | | | |
| IMATI (cm$^2$/m$^2$) | 0.94 | 0.85-1.05 | 0.33 | | | |
| VATI (cm$^2$/m$^2$) | 1.00 | 0.97-1.03 | 0.68 | | | |
| SATI (cm$^2$/m$^2$) | 0.99 | 0.98-1.01 | 0.65 | | | |
| VSR | 1.49 | 0.49-4.46 | 0.47 | | | |
| VAT-RA (HU) | 1.05 | 0.96-1.14 | 0.24 | | | |
| SAT-RA (HU) | 1.04 | 0.99-1.09 | 0.09 | 1.03 | 0.94-1.14 | 0.40 |
| SAT-RA (HU), according to (27) | 2.50 | 0.66-11.01 | 0.15 | | | |

**Table S7:** Main characteristics comparison on day 1 between patients included in the overall Lausanne cohort (n=192) and patients included in the Villejuif external cohort (n=58). Continuous and categorical variables are expressed respectively in median (interquartile range) and N (percentages). Comparisons were performed using the Student's t-test or Mann-Whitney U test for quantitative variables or Chi-Square and Fisher exact tests for categorical variables as appropriate

| | Overall population included in the final analyses (n=192) | External cohort from Villejuif (N=58) | p |
|---|---|---|---|
| **Characteristics** | | | |
| Age (years) | 62.0 (53.2-70.0) | 55.3 (48.7-62.9) | 0.0002 |
| Sex (male) | 141 (73.5) | 46 (79.3) | 0.36 |
| BMI (kg/m$^2$) | 25.8 (22.3-31.2) | 28.0 (24.0-32.0) | 0.09 |
| Ethnicity Causasian Hispanic Other | 161 (83.8) 16 (8.3) 15 (7.8) | 38 (65.5) 11 (19.0) 9 (15.5) | <0.0001 |
| Clinical frailty scale (score) | 4.0 (3.0-4.0) | 3.0 (3.0-4.0) | 0.21 |
| **Aetiology** | | | |
| Alcohol Viral Metabolic Other | 129 (67.2) 34 (17.7) 18 (9.4) 11 (5.7) | 46 (79.3) 3 (5.2) 7 (12.1) 2 (3.5) | 0.02 |
| **Precipitating event** | | | |
| Sepsis Bleeding Other | 79 (41.1) 63 (32.8) 50 (26.1) | 23 (39.7) 16 (27.6) 19 (32.7) | 0.23 |
| **Laboratory on day 1** | | | |
| Leukocytes (G/l) | 15.0 (10.1-20.8) | 11.5 (6.4-14.8) | 0.001 |
| INR | 1.5 (1.3-1.8) | 2.5 (2.1-3.6) | <0.0001 |
| Bilirubin (mg/dl) | 5.3 (3.7-8.2) | 12.8 (4.2-19.6) | <0.0001 |
| AST (IU) | 93.0 (48.0-299.5) | 95.0 (65.0-197.5) | 0.11 |
| Albumin (g/l) | 27.0 (23.2-31.0) | 28.0 (24.0-32.0) | 0.26 |
| Creatinine (mg/dl) | 1.4 (1.0-2.1) | 1.5 (1.2-2.3) | 0.42 |
| Sodium (mmol/l) | 138.0 (134.0-141.0) | 138.0 (134.0-142.0) | 0.93 |
| Lactate (mmol/l) | 4.1 (2.4-7.4) | 2.7 (1.5-4.3) | 0.20 |
| CRP (mg/l) | 55.0 (20.0-112.5) | 35.0 (18.0-72) | 0.02 |
| **ACLF grade on day 1** | | | |
| 0 1 2 3 | 0 (0) 26 (13.6) 59 (30.7) 107 (55.7) | 0 (0) 7 (12.1) 15 (25.9) 36 (62.0) | <0.0001 |
| **Scores on day 1** | | | |
| MELD | 21.9 (15.1-27.9) | 31.0 (25.0-37.0) | <0.0001 |
| CLIF-C ACLF | 67.5 (51.8-72.7) | 77.5 (73.5-82.9) | <0.0001 |
| CLIF-C ACLF-lactate | 71.5 (64.1-80.2) | 78.9 (72.2-87.8) | <0.0001 |
| **Outcome** | | | |
| 28-day survival, % (95%CI) | 58.2 (51.2-65.2) | 41.4 (28.7-54.0) | <0.0001 |
| **Body composition parameters** | | | |
| L3SMI (cm$^2$/m$^2$) | 43.2 (37.1-50.1) | 41.6 (36.2-49.4) | 0.71 |
| Sarcopenia according to L3SMI sex specific cut-offs | 121 (63.0) | 41 (70.7) | 0.25 |
| SMRA (HU) | 36.0 (31.0-41.0) | 30.3 (25.1-37.1) | 0.0004 |
| IMATI (cm$^2$/m$^2$) | 6.3 (3.9-10.0) | 4.0 (3.2-5.2) | <0.0001 |
| VATI (cm$^2$/m$^2$) | 44.3 (24.4-69.9) | 30.4 (14.2-48.7) | <0.0001 |
| SATI (cm$^2$/m$^2$) | 48.6 (27.0-70.3) | 43.6 (29.7-74.6) | 0.48 |
| VSR | 0.9 (0.6-1.4) | 0.7 (0.4-1.1) | 0.009 |
| VAT-RA (HU) | -81.2 (-88.5 to -75.8) | -72.6 (-79.1 to -69.4) | <0.0001 |
| SAT-RA (HU) | -86.6 (-95.7 to -76.8) | -77.6 (-86.1 to -65.5) | <0.0001 |