

Supplementary Materials

- 1. Criteria for cirrhosis diagnosis**
- 2. The detailed protocol of treatment for ACLF**
- 3. Case report form**

1. Criteria for cirrhosis diagnosis

Pathology The gold standard for diagnosing cirrhosis is a liver biopsy performed through a percutaneous or transjugular approach.¹ Ultrasonography was performed 2-4 hours before biopsy. Liver biopsy specimens were taken by experienced physicians. Percutaneous transthoracic puncture of the liver was performed according to standard criteria. After biopsy, patients were kept at the hospital with periodic checks of hematocrit and other vital signs for 24 hours. Cirrhosis was diagnosed according to the globally agreed-upon criteria.² Cirrhosis is defined by its pathological features on microscopy: (a) Presence of parenchymal nodules; (b) Differences in liver cell size and appearance; (c) Fragmentation of the biopsy specimen; (d) Fibrous septa; (e) Altered architecture and vascular relationships. Depending on the size of the nodules, there are three macroscopic types: micronodular, macronodular, and mixed cirrhosis.

Endoscopy Gastroscopy (endoscopic examination of the esophagus, stomach, and duodenum) was performed to exclude the possibility of esophageal and gastric varices.

Radiology Ultrasound is routinely used in the evaluation of cirrhosis.³ Liver size was calculated based on the longitudinal diameter of the right and the left lobes; the ranges of 9-14 cm and 7-10 cm, respectively, are considered normal.⁴ Liver morphology was based on the caudate/right lobe ratio as the former tends to enlarge and the latter to shrink with the progression of cirrhosis. This ratio is considered normal when it is less than 0.6.⁵ Liver boundaries were examined on the inferior surface of the left lobe and the right lobe, especially in the relation to the gallbladder and the right kidney, and described as normal, rounded or nodular.⁶ Liver echogenicity was classified as normal, with increased reflectivity, and coarse and irregular in relation to the echogenicity and the distribution of parenchymal echoes.⁷ Portal vein diameter was measured as the largest anteroposterior diameter at the crossing point with the hepatic artery during

suspended respiration, and values less than 12 mm were considered normal.⁸ Portal vein mean flow velocity was calculated using the pulsed Doppler technique;⁹ the sample volume was taken at the crossing point of the vein with the hepatic artery, and values higher than 15 cm/s were considered normal. Spleen size was assessed according to the longitudinal cross-sectional area as this parameter has been demonstrated to correlate with the actual spleen volume;¹⁰ values up to 45 cm were considered normal². In advanced cirrhosis, the liver may appear small and nodular, with increased echogenicity and irregular-looking areas. Other findings suggestive of cirrhosis in imaging are an enlarged caudate lobe, widening of the liver fissures and enlargement of the spleen. Other radiologic tests include elastography techniques¹¹, abdominal CT and liver/bile duct MRI (MRCP).

Supplementary References

1. Hegarty JE, Williams R. Liver biopsy: techniques, clinical applications, and complications. *Br Med J (Clin Res Ed)* 1984;288(6426):1254-6.
2. Anthony PP, Ishak KG, Nayak NC, et al. The morphology of cirrhosis: definition, nomenclature, and classification. *Bulletin of the World Health Organization* 1977;55(4):521-40. [published Online First: 1977/01/01]
3. Gaiani S, Gramantieri L, Venturoli N, et al. What is the criterion for differentiating chronic hepatitis from compensated cirrhosis? A prospective study comparing ultrasonography and percutaneous liver biopsy. *J Hepatol* 1997;27(6):979-85. [published Online First: 1998/02/07]
4. Niederau C, Sonnenberg A, Muller JE, et al. Sonographic measurements of the normal liver, spleen, pancreas, and portal vein. *Radiology* 1983;149(2):537-40. doi: 10.1148/radiology.149.2.6622701 [published Online First: 1983/11/01]

5. Harbin WP, Robert NJ, Ferrucci JT, Jr. Diagnosis of cirrhosis based on regional changes in hepatic morphology: a radiological and pathological analysis. *Radiology* 1980;135(2):273-83. doi: 10.1148/radiology.135.2.7367613
6. Di Lelio A, Cestari C, Lomazzi A, et al. Cirrhosis: diagnosis with sonographic study of the liver surface. *Radiology* 1989;172(2):389-92. doi: 10.1148/radiology.172.2.2526349
7. Taylor KJ, Gorelick FS, Rosenfield AT, et al. Ultrasonography of alcoholic liver disease with histological correlation. *Radiology* 1981;141(1):157-61. doi: 10.1148/radiology.141.1.6270725
8. Bolondi L, Gandolfi L, Arienti V, et al. Ultrasonography in the diagnosis of portal hypertension: diminished response of portal vessels to respiration. *Radiology* 1982;142(1):167-72. doi: 10.1148/radiology.142.1.7053528
9. Zironi G, Gaiani S, Fenyves D, et al. Value of measurement of mean portal flow velocity by Doppler flowmetry in the diagnosis of portal hypertension. *J Hepatol* 1992;16(3):298-303.
10. Koga T. Correlation between sectional area of the spleen by ultrasonic tomography and actual volume of the removed spleen. *Journal of clinical ultrasound : JCU* 1979;7(2):119-20. [published Online First: 1979/04/01]
11. Foucher J, Chanteloup E, Vergniol J, et al. Diagnosis of cirrhosis by transient elastography (FibroScan): a prospective study. *Gut* 2006;55(3):403-8. doi: 10.1136/gut.2005.069153

2. The detailed treatment protocol for ACLF

All patients received integrated treatment during hospitalization. All enrolled patients received nutritional support therapy, including intravenous high glucose, vitamin, glutathione, adenosylmethionine, or branched-chain amino acids and the use of albumin or plasma for hypoproteinemia. Patients with the HBV pathogen who were HBV-DNA positive immediately received nucleoside analogs (lamivudine alone 100 mg or plus adefovir 10 mg; telbivudine alone 600 mg; entecavir alone 0.5 mg; or telbivudine alone 600 mg per day). A long course of treatment was needed. Patients who actively consumed alcohol were required to abstain. Patients using hepatotoxic drugs were required to stop, and the details of drug use were carefully investigated. Patients with moderate ascites were treated with sodium and water restriction and/or diuretics (anti-mineralocorticoids and/or loop diuretics). Diagnostic abdominocentesis was performed for patients with ascites to determine the presence of spontaneous bacterial peritonitis. Paracentesis combined with intravenous albumin was used for patients with large or refractory ascites. Patients with acute gastrointestinal hemorrhage received intravenous somatostatin, pituitrin, vitamin K and proton pump inhibitors. Urgent therapeutic endoscopy and/or transjugular intrahepatic portosystemic shunting were immediately performed for uncontrolled hemorrhage. Fluid replacement was provided for patients with mean arterial pressure < 70 mmHg, and vasoactive agents were used when necessary. Patients with hepatic encephalopathy were given lactulose, antibiotics, neomycin, sodium benzoate and L-ornithine aspartate; although dietary protein restriction is a cornerstone of therapy, a protein intake of 1-2 g/kg per day is required to maintain an adequate nitrogen balance. Tracheal intubation was performed for patients with hepatic encephalopathy grade III or IV. Patients with bacterial infection were first treated with empirical antibiotic therapy, then the strategy was adjusted immediately

based on bacteria culture and antibiotic sensitivity test. Fungal superinfection was avoided. Patients with renal failure were treated with intravenous albumin or renal replacement therapy. Vasoconstrictors (such as dopamine, noradrenaline, or terlipressin) were an option for patients with refractory hypotension. Patients with $\text{PaO}_2 < 80$ mmHg received persistent low-flow oxygen therapy (2-4 L/min). Mechanical ventilation was chosen according to the severity of respiratory dysfunction. Extracorporeal liver support systems, including albumin dialysis and plasma exchange, were performed as common therapeutic options for ACLF patients if needed.

3. Case report form

No. _____

CASE REPORT FORM

Time of Admission: __ __ / __ __ / __ __

Name: _____

Gender: male female

Age: _____

Telephone: _____

Address: _____

Standard of Admission (only patients who meet item 1 and one of item 2 or 3 can be admitted)

- 1. Hospitalized patients (> 1 day, including patients hospitalized at the ER for observation)
- 2. Chronic hepatitis B patients with severe liver injury (TB \geq 5 mg/dl and INR \geq 1.5)
- 3. Patients who have at least one new symptom in four weeks that is in accordance with the following 4 items:
 - A. Ascites
 - B. Hepatic encephalopathy
 - C. Upper gastrointestinal hemorrhage
 - D. Infection (Lung infection, Urinary system infection, Spontaneous bacterial peritonitis (SBP), Bacteremia or sepsis, Infection of skin or soft tissue, Infection of other parts)

Standard of Exclusion (patients should be excluded if any of the following 6 items applies)

- 1. Patients aged < 18 or > 80 years

- 2. Patients who are pregnant

- 3. Patients who have had hepatocellular carcinoma or other liver malignancies

- 4. Patients who have had any other tumors

- 5. Patients who have had severe extrahepatic diseases
 - COPD combined with respiratory failure

 - Coronary heart disease with 3-level cardiac function

 - Myocardial infarction in the 3 months before hospitalization

 - Failure of renal function due to a chronic renal disease

 - Serious complications of diabetes (causing damage to heart, brain, kidney, feet, etc.)

- 6. Patients receiving immunosuppressive drugs for reasons other than chronic liver diseases (within a year)
 - Chemotherapy against tumor

 - Therapy against connective tissue disease in the active phase

 - Nephrotic syndrome

MEDICAL HISTORY

- **Has the patient has been diagnosed with cirrhosis?**

Yes; a history of __ years No

- **The potential precipitating events (multiple choice):**

- 1. Reactivation or exacerbation of HBV
- 2. Superimposed HAV or HEV infection
- 3. Infections [A. lung infection, B. urinary system infection, C. spontaneous bacterial peritonitis (SBP), D. bacteremia or sepsis, E. infection of skin or soft tissue, F. infection of other parts]
- 4. Alcohol consumption
- 5. Upper gastrointestinal hemorrhage
- 6. Surgery in the past 3 months.
- 7. Hepatotoxic drug use in the past 3 months.
- 8. Unknown

- **Hepatitis B virus infection and past antiviral therapy**

Note the following if the patient has received antiviral therapy with nucleoside analogues (NUCs):

| NUCs | Beginning Time | Ending Time |
|------|----------------|-------------|
| | | |
| | | |
| | | |
| | | |
| | | |

- **Alcohol consumption**

Does the patient have a history of drinking continuously over the past 6 months:

Yes No

The daily average amount consumed: ___ grams of white wine, ___ grams of yellow wine, ___ grams of other wine, ___ bottles of beer

Abstinence from drinking for ___ years

Alcohol consumption during the two weeks before hospitalization:

Yes (for males, average consumption of white wine > 100 grams, yellow wine > 350 grams, other wine > 400 grams, or beer > 2 bottles every day for two weeks; for females, average consumption of white wine > 75 grams, yellow wine > 250 grams, other wine > 250 grams, or beer > 1.5 bottles every day for two weeks)

No

- **Previous decompensation or severe liver injury: Yes No**

Choose the following symptoms if the patient has any (multiple choice):

- Ascites
- Hepatic encephalopathy
- Upper gastrointestinal hemorrhage
- Infections (A. lung infection, B. urinary system infection, C. spontaneous bacterial peritonitis (SBP), D. bacteremia or sepsis, E. infection of skin or soft tissue, F. infection of other parts)
- Severe liver injury (TB \geq 5 mg/dl, and INR \geq 1.5)

- **History of chronic disease (multiple choice):**

Hypertension, Coronary heart disease, Diabetes, Chronic nephrosis, Connective tissue diseases

AT ADMISSION

- **Vital signs**

Temperature: _____°C BP: _____mmHg R: _____/min

Pulse: _____/min

- **Laboratory measurements**

- a) **Blood routine:**

White blood cell count (WBC): _____ *10⁹/L

The proportion of neutrophil granulocyte: (N%): _____%

Hemoglobin concentration(HGB): _____g/L

Hematocrit (HCT): _____%

Platelet count (PLT): _____ *10⁹/L

- b) **Urine routine:**

Protein: white blood cell count (WBC): _____/HP

Red blood cell count (RBC): _____/HP

- c) **Feces routine:**

Color: _____

Occult blood (OB): _____

- d) **Analysis of liver function, renal function, blood glucose, electrolytes, and blood vigor:**

Alanine aminotransferase (ALT): _____ U/L

Aspartate transaminase (AST): _____ U/L

Alkaline phosphatase (AKP): _____ U/L

γ -glutamyl transpeptidase (γ -GGT): _____ U/L

Total bilirubin (TB): _____mg/dL

Albumin (ALB): _____g/L

Serum creatinine (Cr): _____mg/dl

Serum sodium (Na⁺): _____mmol/L

Serum potassium (K⁺): _____mmol/L

PH: _____

PCO₂: _____KPa

PO₂: _____KPa

Blood lactic acid: _____mmol/L

Blood ammonia: _____mmol/L

Fasting blood-glucose (GLU): _____mmol/L

C-reactive protein (CRP): _____mg/L

Alpha fetoprotein (AFP): _____µg/L

Ferritin: _____µg/L

e) **Coagulation:**

Prothrombin time (PT): _____s

International normalized ratio (INR): _____

• **Hepatitis B virus index**

HBV-DNA: _____copies/ml

The five-index hepatitis B (HBsAg/HBsAb/HBcAb/HBeAg/HBeAb):

HCV-RNA: Yes _____copies/ml No

Hepatitis A virus antibody (IgM/IgG): _____

Hepatitis E virus antibody (IgM/IgG): _____

• **Ascites:** Yes No

Diuretics use Yes No

Ascites can be controlled with drugs Yes No

Paracentesis Yes No

SBP: multiple nuclear cells: _____*10⁶/L

Proportion of neutrophil granulocytes: _____%

Proportion of multiple nuclear cells * neutrophil granulocytes: 250 *
10⁶/L < 250 * 10⁶/L

- **Infection**

Bacterial infection: Yes No

SIRS: Yes (in accordance with at least 2 of the following 4 items)

1. Body temperature > 38°C or < 36°C

2. Heart rate > 90/min

3. Breathing > 20 times/min or PaCO₂ < 32 mmHg

4. White blood cell count > 12×10⁹/L or <4×10⁹/L (or immature
granulocytes > 10%)

No

Sepsis: Yes (infection with SIRS) No

Septic shock: Yes (sepsis and systolic pressure < 90 mmHg or MAP < 60 mmHg)

No

- **Imagological examination**

- a) **Lung infection**

1. Lung infection Yes No

2. Basis of the diagnosis:

X-ray: _____

Date: __ __/__ __/__ __

CT: _____

Date __ __/__ __/__ __

3. Infected parts: _____

- b) **Fibrosis**

FibroScan/FibroTouch (liver stiffness measurement, LSM): __KPa

Date: __ __/__ __/__ __

- c) **Cirrhosis**

Imaging findings of cirrhosis Yes No

CT examination: _____

Date: __ __/__ __/__ __

Ultrasound: _____

Date: __ __/__ __/__ __

- **Organ failure**

- a) **Liver function:**

TB: _____mg/dl

Liver failure: Yes [TB \geq 12 mg/dl] No

- b) **Coagulation function:**

INR: _____

Coagulation function failure:

Yes (INR \geq 2.5) No

- c) **Renal function:**

Renal supportive treatment (hemodialysis) provided: Yes No

Renal failure:

Yes (serum creatinine \geq 2 mg/dl or renal supportive treatment) No

- d) **Cerebral function:**

Hepatic encephalopathy grading (Hepatic encephalopathy Phase 0 is not within the scope of the evaluation):

Phase I Phase II Phase III Phase IV

Cerebral failure:

Yes (hepatic encephalopathy higher than or equal to Level 3) No

- e) **Circulatory function:**

Heart rate: _

Vasopressors required to maintain basic blood pressure:

Yes [epinephrine (E)___mg/kg/min, norepinephrine (NE)___mg/kg/min and dopamine (DA)___mg/kg/min], blood pressure: __/ __mmHg

No, blood pressure: __/ __mmHg

Circulatory failure:

Yes (vasopressor is needed) No

f) **Lung function:**

Oxyhemoglobin saturation (SpO₂): _____%

Fraction of inspired oxygen (FiO₂): _____%

SPO₂/FiO₂: _____

Need for mechanical ventilation: Yes No

Lung failure:

Yes (SPO₂/FiO₂ < 214 or mechanical ventilation) No

- **Emergency (post-enrollment ACLF)**

Yes

No

If “Yes”, please complete the following table:

| Date | Liver failure 1: Yes 2: No | Coagulation failure 1: Yes 2: No | Kidney failure 1: Yes 2: No | Cerebral failure 1: Yes 2: No | Circulation failure 1: Yes 2: No | Lung failure 1: Yes 2: No | ACLF 1: Yes 2: No |
|------|----------------------------------|--|-----------------------------------|-------------------------------------|--|---------------------------------|-------------------------|
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |

- **Condition of enrolled patient**

| Date | Recovered 1: Yes 2: No | No change 1: Yes 2: No | Worsened 1: Yes 2: No | Died 1: Yes 2: No |
|------|------------------------------|------------------------------|-----------------------------|-------------------------|
| | | | | |
| | | | | |
| | | | | |

DAY 4 AFTER ADMISSION

- **Vital signs**

Temperature: _____°C BP: _____mmHg R: _____/min

Pulse: _____/min

- **Laboratory measurements**

- a) **Blood routine:**

White blood cell count (WBC): _____ *10⁹/L

Proportion of neutrophil granulocytes: (N%): _____%

Hemoglobin concentration (HGB): _____g/L

Hematocrit (HCT): _____%

Platelet count (PLT): _____ *10⁹/L

- b) **Urine routine:**

Protein: white blood cell count (WBC): _____/HP

Red blood cell count (RBC): _____/HP

- c) **Feces routine:**

Color: _____

Occult blood (OB): _____

- d) **Analysis of liver function, renal function, blood glucose, electrolytes, and blood vigor:**

Alanine aminotransferase (ALT): _____ U/L

Aspartate transaminase (AST): _____ U/L

Alkaline phosphatase (AKP): _____ U/L

γ -glutamyl transpeptidase (γ -GGT): _____ U/L

Total bilirubin (TB): _____ mg/dL

Albumin (ALB): _____ g/L

Serum creatinine (Cr): _____mg/dl

Serum sodium (Na⁺): _____mmol/L

Serum potassium (K⁺): _____mmol/L

PH: _____

PCO₂: _____KPa

PO₂: _____KPa

Blood lactic acid: _____mmol/L

Blood ammonia: _____mmol/L

Fasting blood glucose (GLU): _____mmol/L

C-reactive protein (CRP): _____mg/L

Alpha fetoprotein (AFP): _____μg/L

Ferritin: _____μg/L

e) Coagulation:

Prothrombin time (PT): _____s

International normalized ratio (INR): _____

- **Organ failure**

- a) **Liver function:**

TB: _____mg/dl

Liver failure: Yes [TB \geq 12 mg/dl] No

- b) **Coagulation function:**

INR: _____

Coagulation function failure:

Yes (INR \geq 2.5) No

- c) **Renal function:**

Provision of renal supportive treatment (hemodialysis): Yes No

Renal failure:

Yes (serum creatinine \geq 2 mg/dl or renal supportive treatment) No

- d) **Cerebral function:**

Hepatic encephalopathy grading (Hepatic encephalopathy Phase 0 is not within the scope of the evaluation):

Phase I Phase II Phase III Phase IV

Cerebral failure:

Yes (hepatic encephalopathy higher than or equal to Level 3) No

- e) **Circulatory function:**

Heart rate: _

Vasopressors required to maintain basic blood pressure:

Yes [epinephrine (E)___mg/kg/min, norepinephrine (NE)___mg/kg/min and dopamine (DA)___mg/kg/min], blood pressure: __/ __mmHg

No, blood pressure: __/ __mmHg

Circulatory failure:

Yes (vasopressor is needed) No

f) **Lung function:**

Oxyhemoglobin saturation (SpO₂): _____%

Fraction of inspired oxygen (FiO₂): _____%

SPO₂/FiO₂: _____

Need for mechanical ventilation: Yes No

Lung failure:

Yes (SPO₂/FiO₂ < 214 or need for mechanical ventilation) No

- **Emergency (post-enrollment ACLF)**

Yes

No

If “Yes”, please complete the following table:

| Date | Liver failure 1: Yes 2: No | Coagulation failure 1: Yes 2: No | Kidney failure 1: Yes 2: No | Cerebral failure 1: Yes 2: No | Circulation failure 1: Yes 2: No | Lung failure 1: Yes 2: No | ACLF 1: Yes 2: No |
|------|----------------------------------|--|-----------------------------------|-------------------------------------|--|---------------------------------|-------------------------|
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |

- **Condition of enrolled patient**

| Date | Recovered 1: Yes 2: No | No change 1: Yes 2: No | Worsened 1: Yes 2: No | Died 1: Yes 2: No |
|------|------------------------------|------------------------------|-----------------------------|-------------------------|
| | | | | |
| | | | | |
| | | | | |

DAY 7 AFTER ADMISSION

- **Vital signs**

Temperature: _____°C BP: _____mmHg R: _____/min

Pulse: _____/min

- **Laboratory measurements**

- a) **Blood routine:**

White blood cell count (WBC): _____ *10⁹/L

Proportion of neutrophil granulocytes: (N%): _____%

Hemoglobin concentration (HGB): _____g/L

Hematocrit (HCT): _____%

Platelet count (PLT): _____ *10⁹/L

- b) **Urine routine:**

Protein: white blood cell count (WBC): _____/HP

Red blood cell count (RBC): _____/HP

- c) **Feces routine:**

Color: _____

Occult blood (OB): _____

- d) **Analysis of liver function, renal function, blood glucose, electrolytes, and blood vigor:**

Alanine aminotransferase (ALT): _____ U/L

Aspartate transaminase (AST): _____ U/L

Alkaline phosphatase (AKP): _____ U/L

γ -glutamyl transpeptidase (γ -GGT): _____ U/L

Total bilirubin (TB): _____ mg/dL

Albumin (ALB): _____ g/L

Serum creatinine (Cr): _____mg/dl

Serum sodium (Na⁺): _____mmol/L

Serum potassium (K⁺): _____mmol/L

PH: _____

PCO₂: _____KPa

PO₂: _____KPa

Blood lactic acid: _____mmol/L

Blood ammonia: _____mmol/L

Fasting blood-glucose (GLU): _____mmol/L

C-reactive protein (CRP): _____mg/L

Alpha fetoprotein (AFP): _____μg/L

Ferritin: _____μg/L

e) Coagulation:

Prothrombin time (PT): _____s

International normalized ratio (INR): _____

- **Organ failure**

- a) **Liver function:**

TB: _____mg/dl

Liver failure: Yes [TB \geq 12 mg/dl] No

- b) **Coagulation function:**

INR: _____

Coagulation function failure:

Yes (INR \geq 2.5) No

- c) **Renal function:**

Provision of renal supportive treatment (hemodialysis): Yes No

Renal failure:

Yes (serum creatinine \geq 2 mg/dl or renal supportive treatment) No

- d) **Cerebral function:**

Hepatic encephalopathy grading (hepatic encephalopathy Phase 0 is not within the scope of the evaluation):

Phase I Phase II Phase III Phase IV

Cerebral failure:

Yes (hepatic encephalopathy higher than or equal to Level 3) No

- e) **Circulatory function:**

Heart rate: _

Vasopressors required to maintain basic blood pressure

Yes [epinephrine (E)___mg/kg/min, norepinephrine (NE)___mg/kg/min and dopamine (DA)___mg/kg/min], blood pressure: __/ __mmHg

No, blood pressure: __/ __mmHg

Circulatory failure:

Yes (vasopressor is needed) No

f) **Lung function:**

Oxyhemoglobin saturation (SpO₂): _____%

Fraction of inspired oxygen (FiO₂): _____%

SPO₂/FiO₂: _____

Need for mechanical ventilation: Yes No

Lung failure:

Yes (SPO₂/FiO₂ < 214 or need for mechanical ventilation) No

- **Emergency (post-enrollment ACLF)**

Yes

No

If “Yes”, please complete the following table:

| Date | Liver failure 1: Yes 2: No | Coagulation failure 1: Yes 2: No | Kidney failure 1: Yes 2: No | Cerebral failure 1: Yes 2: No | Circulation failure 1: Yes 2: No | Lung failure 1: Yes 2: No | ACLF 1: Yes 2: No |
|------|----------------------------------|--|-----------------------------------|-------------------------------------|--|---------------------------------|-------------------------|
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |

- **Condition of enrolled patient**

| Date | Recovered 1: Yes 2: No | No change 1: Yes 2: No | Worsened 1: Yes 2: No | Died 1: Yes 2: No |
|------|------------------------------|------------------------------|-----------------------------|-------------------------|
| | | | | |
| | | | | |
| | | | | |

DAY 14 AFTER ADMISSION

- **Vital signs**

Temperature: _____°C BP: _____mmHg R: _____/min

Pulse: _____/min

- **Laboratory measurements**

- a) **Blood routine:**

White blood cell count (WBC): _____ *10⁹/L

Proportion of neutrophil granulocytes: (N%): _____%

Hemoglobin concentration (HGB): _____g/L

Hematocrit (HCT): _____%

Platelet count (PLT): _____ *10⁹/L

- b) **Urine routine:**

Protein: white blood cell count (WBC): _____/HP

Red blood cell count (RBC): _____/HP

- c) **Feces routine:**

Color: _____

Occult blood (OB): _____

- d) **Analysis of liver function, renal function, blood glucose, electrolytes, and blood vigor:**

Alanine aminotransferase (ALT): _____ U/L

Aspartate transaminase (AST): _____ U/L

Alkaline phosphatase (AKP): _____ U/L

γ -glutamyl transpeptidase (γ -GGT): _____ U/L

Total bilirubin (TB): _____ mg/dL

Albumin (ALB): _____ g/L

Serum creatinine (Cr): _____mg/dl

Serum sodium (Na⁺): _____mmol/L

Serum potassium (K⁺): _____mmol/L

PH: _____

PCO₂: _____KPa

PO₂: _____KPa

Blood lactic acid: _____mmol/L

Blood ammonia: _____mmol/L

Fasting blood-glucose (GLU): _____mmol/L

C-reactive protein (CRP): _____mg/L

Alpha fetoprotein (AFP): _____μg/L

Ferritin: _____μg/L

e) Coagulation:

Prothrombin time (PT): _____s

International normalized ratio (INR): _____

- **Organ failure**

a) **Liver function:**

TB: _____mg/dl

Liver failure: Yes [TB \geq 12 mg/dl] No

b) **Coagulation function:**

INR: _____

Coagulation function failure:

Yes (INR \geq 2.5) No

c) **Renal function:**

Provision of renal supportive treatment (hemodialysis): Yes No

Renal failure:

Yes (serum creatinine \geq 2 mg/dl or renal supportive treatment) No

d) **Cerebral function:**

Hepatic encephalopathy grading (hepatic encephalopathy Phase 0 is not within the scope of the evaluation):

Phase I Phase II Phase III Phase IV

Cerebral failure:

Yes (hepatic encephalopathy higher than or equal to Level 3) No

e) **Circulatory function:**

Heart rate: _

Need for vasopressors to maintain basic blood pressure:

Yes [epinephrine (E)___mg/kg/min, norepinephrine (NE)___mg/kg/min and dopamine (DA)___mg/kg/min], blood pressure: __/ __mmHg

No, blood pressure: __/ __mmHg

Circulatory failure:

Yes (vasopressor is needed) No

f) **Lung function:**

Oxyhemoglobin saturation (SpO₂): _____%

Fraction of inspired oxygen (FiO₂): _____%

SPO₂/FiO₂: _____

Need for mechanical ventilation: Yes No

Lung failure:

Yes (SPO₂/FiO₂ < 214 or need for mechanical ventilation) No

- **Emergency (post-enrollment ACLF)**

Yes

No

If “Yes”, please complete the following table:

| Date | Liver failure 1: Yes 2: No | Coagulation failure 1: Yes 2: No | Kidney failure 1: Yes 2: No | Cerebral failure 1: Yes 2: No | Circulation failure 1: Yes 2: No | Lung failure 1: Yes 2: No | ACLF 1: Yes 2: No |
|------|----------------------------------|--|-----------------------------------|-------------------------------------|--|---------------------------------|-------------------------|
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |

- **Condition of enrolled patient**

| Date | Recovered 1: Yes 2: No | No change 1: Yes 2: No | Worsened 1: Yes 2: No | Died 1: Yes 2: No |
|------|------------------------------|------------------------------|-----------------------------|-------------------------|
| | | | | |
| | | | | |
| | | | | |

DAY 21 AFTER ADMISSION

- **Vital signs**

Temperature: _____°C BP: _____mmHg R: _____/min

Pulse: _____/min

- **Laboratory measurements**

- a) **Blood routine:**

White blood cell count (WBC): _____ *10⁹/L

Proportion of neutrophil granulocytes: (N%): _____%

Hemoglobin concentration (HGB): _____g/L

Hematocrit (HCT): _____%

Platelet count (PLT): _____ *10⁹/L

- b) **Urine routine:**

Protein: white blood cell count (WBC): _____/HP

Red blood cell count (RBC): _____/HP

- c) **Feces routine:**

Color: _____

Occult blood (OB): _____

- d) **Analysis on liver function, renal function, blood glucose, electrolytes, and blood vigor:**

Alanine aminotransferase (ALT): _____ U/L,

Aspartate transaminase (AST): _____ U/L

Alkaline phosphatase (AKP): _____ U/L

γ -glutamyl transpeptidase (γ -GGT): _____ U/L

Total bilirubin (TB): _____ mg/dL

Albumin (ALB): _____ g/L

Serum creatinine (Cr): _____mg/dl

Serum sodium (Na⁺): _____mmol/L

Serum potassium (K⁺): _____mmol/L

PH: _____

PCO₂: _____KPa

PO₂: _____KPa

Blood lactic acid: _____mmol/L

Blood ammonia: _____mmol/L

Fasting blood-glucose (GLU): _____mmol/L

C-reactive protein (CRP): _____mg/L

Alpha fetoprotein (AFP): _____μg/L

Ferritin: _____μg/L

e) Coagulation:

Prothrombin time (PT): _____s

International normalized ratio (INR): _____

- **Organ failure**

a) **Liver function:**

TB: _____mg/dl

Liver failure: Yes [TB \geq 12 mg/dl] No

b) **Coagulation function:**

INR: _____

Coagulation function failure:

Yes (INR \geq 2.5) No

c) **Renal function:**

Provision of renal supportive treatment (hemodialysis): Yes No

Renal failure:

Yes (serum creatinine \geq 2 mg/dl or renal supportive treatment) No

d) **Cerebral function:**

Hepatic encephalopathy grading (Hepatic encephalopathy Phase 0 is not within the scope of the evaluation):

Phase I Phase II Phase III Phase IV

Cerebral failure:

Yes (hepatic encephalopathy higher than or equal to Level 3) No

e) **Circulatory function:**

Heart rate: _

Need for vasopressors to maintain basic blood pressure:

Yes [epinephrine (E)___mg/kg/min, norepinephrine (NE)___mg/kg/min and dopamine (DA)___mg/kg/min], blood pressure: ___/___mmHg

No, blood pressure: ___/___mmHg

Circulatory failure:

Yes (vasopressor is needed) No

f) **Lung function:**

Oxyhemoglobin saturation (SpO_2): _____%

Fraction of inspired oxygen (FiO_2): _____%

SPO_2/FiO_2 : _____

Need for mechanical ventilation: Yes No

Lung failure:

Yes ($SPO_2/FiO_2 < 214$ or need for mechanical ventilation) No

- **Emergency (post-enrollment ACLF)**

Yes

No

If “Yes”, please complete the following table:

| Date | Liver failure 1: Yes 2: No | Coagulation failure 1: Yes 2: No | Kidney failure 1: Yes 2: No | Cerebral failure 1: Yes 2: No | Circulation failure 1: Yes 2: No | Lung failure 1: Yes 2: No | ACLF 1: Yes 2: No |
|------|----------------------------------|--|-----------------------------------|-------------------------------------|--|---------------------------------|-------------------------|
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |

- **Condition of enrolled patient**

| Date | Recovered 1: Yes 2: No | No change 1: Yes 2: No | Worsened 1: Yes 2: No | Died 1: Yes 2: No |
|------|------------------------------|------------------------------|-----------------------------|-------------------------|
| | | | | |
| | | | | |
| | | | | |

DAY 28 AFTER ADMISSION

- **Vital signs**

Temperature: _____°C BP: _____mmHg R: _____/min

Pulse: _____/min

- **Laboratory measurements**

- a) **Blood routine:**

White blood cell count (WBC): _____ *10⁹/L

Proportion of neutrophil granulocytes: (N%): _____%

Hemoglobin concentration (HGB): _____g/L

Hematocrit (HCT): _____%

Platelet count (PLT): _____ *10⁹/L

- b) **Urine routine:**

Protein: white blood cell count (WBC): _____/HP

Red blood cell count (RBC): _____/HP

- c) **Feces routine:**

Color: _____

Occult blood (OB): _____

- d) **Analysis of liver function, renal function, blood glucose, electrolytes, and blood vigor:**

Alanine aminotransferase (ALT): _____ U/L

Aspartate transaminase (AST): _____ U/L

Alkaline phosphatase (AKP): _____ U/L

γ -glutamyl transpeptidase (γ -GGT): _____ U/L

Total bilirubin (TB): _____ mg/dL

Albumin (ALB): _____ g/L

Serum creatinine (Cr): _____mg/dl

Serum sodium (Na⁺): _____mmol/L

Serum potassium (K⁺): _____mmol/L

PH: _____

PCO₂: _____KPa

PO₂: _____KPa

Blood lactic acid: _____mmol/L

Blood ammonia: _____mmol/L

Fasting blood-glucose (GLU): _____mmol/L

C-reactive protein (CRP): _____mg/L

Alpha fetoprotein (AFP): _____μg/L

Ferritin: _____μg/L

e) Coagulation:

Prothrombin time (PT): _____s

International normalized ratio (INR): _____

- **Organ failure**

- a) **Liver function:**

TB: _____mg/dl

Liver failure: Yes [TB \geq 12 mg/dl] No

- b) **Coagulation function:**

INR: _____

Coagulation function failure:

Yes (INR \geq 2.5) No

- c) **Renal function:**

Provision of renal supportive treatment (hemodialysis): Yes No

Renal failure:

Yes (serum creatinine \geq 2 mg/dl or renal supportive treatment) No

- d) **Cerebral function:**

Hepatic encephalopathy grading (hepatic encephalopathy Phase 0 is not within the scope of the evaluation):

Phase I Phase II Phase III Phase IV

Cerebral failure:

Yes (hepatic encephalopathy higher than or equal to Level 3) No

- e) **Circulatory function:**

Heart rate: _

Need for vasopressors to maintain basic blood pressure:

Yes [epinephrine (E)___mg/kg/min, norepinephrine (NE)___mg/kg/min and dopamine (DA)___mg/kg/min], blood pressure: __/ __mmHg

No, blood pressure: __/ __mmHg

Circulatory failure:

Yes (vasopressor is needed) No

f) **Lung function:**

Oxyhemoglobin saturation (SpO₂): _____%

Fraction of inspired oxygen (FiO₂): _____%

SPO₂/FiO₂: _____

Whether mechanical ventilation is needed: Yes No

Lung failure:

Yes (SPO₂/FiO₂ < 214 or need for mechanical ventilation) No

- **Emergency (post-enrollment ACLF)**

Yes

No

If “Yes”, please complete the following table:

| Date | Liver failure 1: Yes 2: No | Coagulation failure 1: Yes 2: No | Kidney failure 1: Yes 2: No | Cerebral failure 1: Yes 2: No | Circulation failure 1: Yes 2: No | Lung failure 1: Yes 2: No | ACLF 1: Yes 2: No |
|------|----------------------------------|--|-----------------------------------|-------------------------------------|--|---------------------------------|-------------------------|
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |

- **Condition of enrolled patient**

| Date | Recovered 1: Yes 2: No | No change 1: Yes 2: No | Worsened 1: Yes 2: No | Died 1: Yes 2: No |
|------|------------------------------|------------------------------|-----------------------------|-------------------------|
| | | | | |
| | | | | |
| | | | | |

DISCHARGE REGISTRATION

• **Date:** __ __/__ __/__ __

• **Liver transplantation**

Yes; date: __ __/__ __/__ __ No

• **Death**

Yes; date: __ __/__ __/__ __ No

Main cause of death:

Multiple organ failure without septic or hypovolemic shock

Multiple organ failure with septic

Multiple organ failure with hypovolemic shock

Septic

Hypovolemic shock

Other causes

Unknown

TWENTY-EIGHT-DAY FOLLOW-UP

- **Death**

Yes; date: __ __/__ __/__ __ No

Main cause of death:

- Multiple organ failure without septic or hypovolemic shock
- Multiple organ failure with septic
- Multiple organ failure with hypovolemic shock
- Septic
- Hypovolemic shock
- Other causes
- Unknown

NINETY-DAY FOLLOW-UP

- **Death**

Yes; date: __ __/__ __/__ __ No

Main cause of death:

- Multiple organ failure without septic or hypovolemic shock
- Multiple organ failure with septic
- Multiple organ failure with hypovolemic shock
- Septic
- Hypovolemic shock
- Other causes
- Unknown