

## **Improving survival of acute-on-chronic liver failure patients complicated with invasive pulmonary aspergillosis**

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**Supplementary tables**

**Table s1. Demographic, clinical and biochemical characteristics of patients at the time of IPA diagnosis according to CLIF-SOFA lungs core.**

Characteristic	Higher lung score (>1) (n=7)	Lower lung score (<2) (n=13)	p value
Age (years)	41 [31, 70]	43 [26, 58]	0.578
Male (n, %)	6 (85.7)	12 (93.2)	1
Time from enrolment to IPA diagnosis (days)	18 [0, 33]	12 [0, 44]	0.780
Time from fever to IPA diagnosis (days)*	6.5 [2.0, 14.0]	4.0 [1.0, 14.0]	0.237
Fever (n, %)	7 (100)	11 (84.6)	0.521
Other infection (n, %)	1 (14.2)	3 (23.1)	1
Voriconazole treatment (n, %)	3 (42.9)	11 (84.6)	0.122
Radiological features			
Well-shaped nodule(s) with halo sign (n,%)	0 (0)	3 (23.1)	0.521
Well-shaped nodule(s) without halo sign (n,%)	5 (71.4)	10 (76.9)	1
Air-crescent sign (n,%)	0/7	0/13	-
Cavitation (n,%)	1 (14.3)	0 (0)	0.350
Masses/consolidation (n,%)	6 (85.7)	3 (23.1)	0.017
Pleural fluid (n,%)	2 (28.6)	5 (38.5)	0.526
Bilateral lung infection (n,%)	7 (100)	11 (84.6)	0.521
C-reactive protein (mg/L)	30.0 [16.0, 52.6]	35.3 [3.0, 69.4]	1.000
Procalcitonin (ng/mL)	1.3 [0.9, 1.9]	1.0 [0.2, 3.1]	0.524
Leukocyte count (10 <sup>9</sup> /L)	16.8 [6.1, 23.0]	15.0 [3.6, 34.7]	0.861
Platelet count (10 <sup>9</sup> /L)	57 [27, 100]	54 [24, 199]	0.693
Total bilirubin (mg/dL)	28.8 [9.7, 47.3]	24.9 [16.7, 46.1]	0.285
Aspartate aminotransferase (U/L)	175.9 [35.0, 209.0]	87.5 [32.0, 279.3]	0.108
Alanine aminotransferase (U/L)	75.6 [49.5, 194.0]	74.7 [15.0, 197.2]	0.735
International normalized ratio	2.8 [1.8, 4.6]	2.4 [1.5, 3.5]	0.104
Albumin (mg/L)	25.4 [22.7, 37.4]	34.8 [20.9, 40.3]	0.446
Creatinine (mg/L)	1 [0.5, 2.8]	0.7 [0.4, 2.2]	0.122
Serum sodium (mmol/L)	128 [123, 139]	135 [130, 140]	0.032
PSI <sup>16</sup>	109 [81, 169]	83 [46, 118]	0.005
CURB-65 <sup>16</sup>	1 [0, 3]	1 [0, 2]	0.097
MELD <sup>15</sup>	33.3 [18.4, 40.9]	23.8 [15.4, 37.6]	0.052
MELD-Na <sup>15</sup>	37.7 [25.1, 60.0]	27.6 [15.4, 45.6]	0.008
CLIF-C ACLFs <sup>15</sup>	44.18 [29.4, 57.1]	50.53 [47.0, 72.6]	0.008
CLIF-SOFA <sup>1</sup>	12 [10, 15]	8 [6, 11]	0.002
Cerebral failure (n, %)	3 (42.9)	0 (0)	0.031
Liver failure (n, %)	6 (85.7)	13 (100)	0.350
Lung failure (n, %)	3 (42.9)	0 (0)	0.031
Coagulation failure (n, %)	5 (71.4)	6 (46.2)	0.374
Kidney failure (n, %)	1 (14.3)	1 (7.7)	1
Circulation failure (n, %)	0 (0)	0 (0)	-

Data are expressed as the median [min-max] for continuous variables and counts (percentage) for categorical variables.

MELD: Model for end-stage liver disease.

CLIF-SOFA: Chronic Liver Failure-Sequential Organ Failure Assessment.

\*Patients with fever before diagnosis are compared.

**Table s2. ICD-10 codes for related diseases for patient screening.**

Disease	ICD-10 code
<b>Related to liver failure</b>	
Acute alcoholic hepatic failure	K70.401
Acute drug induced hepatic failure	K71.102
Acute hepatic failure	K72.000
Acute liver function failure	K72.003
Sub-acute drug-induced hepatic failure	K71.104
Sub-acute hepatic failure	K72.001
Chronic hepatic failure	K72.100
Chronic alcoholic hepatic failure	K70.402
Hepatic failure, nospecified	K72.900
<b>Related to lung infections</b>	
Lung infection	J98.414
Pneumonia	J18.900
Pulmonary fungal infection	B49. x14
Pulmonary aspergillosis	B44.100+J99.8*

Note: Patients diagnosed with “Acute-on-chronic liver failure” without ICD-10 code records were also screened, since acute-on-chronic liver failure has no related ICD-10 code yet.

**Table s3.** The adapted diagnostic criteria for IA based on EORTC/MSG and AspICU criteria.

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**Probable IA (all three criteria must be met)**

- Host risk factor: ACLF is considered a risk factor
- Clinical features: radiological features (dense, well-circumscribed lesion (s) with or without a halo sign, air crescent sign or cavity, mass(es))
- Mycological criteria: direct test (cytology, direct microscopy, or culture) indicating the presence of *Aspergillus* species or galactomannan antigen detected in plasma

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**Possible IA**

- Presence of host factor and radiological features (dense, well-circumscribed lesion (s) with or without a halo sign, air crescent sign and cavity, masses), but in the absence of mycological criteria
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