

中文題目：慢性肝病急性發作 28 天死亡率及預測因子

英文題目：The incidence and predictors of 28-day mortality in patients with acute on chronic liver failure

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Background: The characteristics of acute-on-chronic liver failure included its association with a systemic inflammatory response, organ failures, and high 28-day mortality. Multiple scoring systems were developed to predict the short-term outcomes. However, there is a paucity of studies that determine the prognostic factors for patients with ACLF in Taiwan. The aim of our study is to analyze clinical characters and determine prognostic factors in patients with ACLF.

Method: The cohort study was conducted based on Chang Gung Research Database (CGRD). We enrolled the patients with ACLF in Kaohsiung CGMH between January 2009 and December 2018. Patients who met the definition of ACLF defined by Asian Pacific Association for the Study of the Liver (APASL) were enrolled. A total of 231 patients with ACLF were included in the study. Parameters at baseline and at Day 3-6 were used to calculate the following prognostic scores: CLIF-C ACLF score, COSSH-ACLF score, MELD 3.0 score, and Child-Pugh score.

Results: Among 231 patients with ACLF, 26 patients received liver transplantation (LT). Hepatitis B reactivation is the predominant cause of acute hepatic insult, accounts for 68 percent, followed by alcohol abuse, drug or herb induced liver failure, and autoimmune hepatitis flare. The 28-day mortality rate in LT-free patients were 31%, but all LT patients survived the first month. The multivariate analysis demonstrated that older age, high INR, higher serum bilirubin, and severe hepatic encephalopathy were independent predictors for 28-day mortality in LT-free patients. The CLIF-C ACLF score and COSSH-ACLF score at Day 3-6 exhibited good predictive value for 28-day mortality, the AUC values were above 0.9. The CLIF-C ACLF score at Day 3-6 showed the highest predictive value, and the optimal cutoff value was 47. Patients with a CLIF-C ACLF score at Day 3-6 below the threshold of 47 had a 28-day mortality of only 7%, which was significantly lower than in patients with CLIF-C ACLF score above 47 (76%). No one survived with a CLIF-C ACLF score above the threshold of 63 in patients without liver transplant.

Conclusion: CLIF-C ACLF score and COSSH ACLF score based on parameters at Day 3-6 can accurately predict short-term mortality in patients with ACLF and might be used to guide clinical management.

Table 1. Patient's demographics and baseline characteristics with ACLF

Table	Variable, mean (SD)	LT-free (205)	LT (26)	p value	2.
	Age (years)	53.4 (12.7)	49.1 (7.5)	0.017	
	Men, n (%)	157 (76.6)	21 (80.8)	0.806	
	Liver cirrhosis, n (%)	117 (57.1)	18 (69.2)	0.293	
	Diabetes mellitus, n (%)	52 (25.4)	4 (15.4)	0.336	
	Hypertension, n (%)	65 (31.7)	6 (23.1)	0.499	
	Causes				
	Hepatitis B infection, n (%)	133 (64.9)	25 (96.2)		
	Alcohol, n (%)	47 (22.9)	1 (3.8)		
	Drug or herb, n (%)	11 (5.4)	0 (0)		
	Autoimmune, n (%)	5 (2.4)	0 (0)		
	Others, n (%)	9 (4.4)	0 (0)		
	Hemoglobin (g/dL)	12.7 (3.2)	13.4 (2.3)	0.225	
	WBC count (10 ³ /uL)	8.9 (5.0)	7.9 (4.5)	0.344	
	Platelet count (10 ³ /uL)	130.1 (75.3)	135.5 (48.8)	0.609	
	INR	2.12 (0.85)	2.26 (0.62)	0.364	
	Asparate aminotransaminase (U/L)	1040 (1102)	1566 (1047)	0.031*	
	Alanine aminotransaminase (U/L)	1094 (1215)	1810 (995)	0.003*	
	Total bilirubin (mg/dL)	14.0 (8.5)	13.9 (8.2)	0.960	
	Albumin (g/dL)	2.97 (0.57)	2.94 (0.57)	0.846	
	Creatinine (mg/dL)	1.32 (1.58)	0.96 (0.63)	0.054	
	Sodium (mEq/L)	134.5 (5.3)	135.5 (3.8)	0.305	
	28-day mortality	31%	0%	0.002*	
	90-day mortality	43%	4%	<0.001*	

Clinical parameters at baseline according to survival status at Day 28

Variable, mean (SD)	Survivor	Non-survivor	p value
Age (years)	50.71(12.8)	58.9(14.3)	<0.001*
CLIF-C OF score	8.1(1.5)	9.3(1.86)	<0.001*
CLIF-C ACLF score	40(7)	48(8)	<0.001*
COSSH-ACLF score	5.7(0.8)	6.9(1.3)	<0.001*
MELD 3.0 score	27(6)	32(8)	<0.001*
Child-Pugh classification A/B/C (%)	2.9/42.3/54.7	1.6/19/79.4	0.004*
WBC count (10 ³ /uL)	8.8 (5.2)	9.1 (4.7)	0.690
Platelet count (10 ³ /uL)	129 (78)	127 (67)	0.897
INR	1.88 (0.55)	2.67 (1.11)	<0.001*
Total bilirubin (mg/dL)	12.8 (7.8)	16.1 (9.5)	0.014*

Albumin (g/dL)	2.98 (0.59)	2.89 (0.52)	0.368
Creatinine (mg/dL)	1.23 (1.30)	1.54 (2.10)	0.225
Sodium (mEq/L)	134.1 (5.2)	135.2 (5.4)	0.201

Table 3. Uni- and multivariate analysis of factors at baseline associated with 28-day mortality in LT-free patients

Figure 1. Enrollment of patients according to APASL criteria

	Univariate			Multivariate		
	HR	95%CI	p value	HR	95%CI	p value
Sex (male/female)	1.215	0.696-2.119	0.493			
Age (year)	1.037	1.019-1.057	<0.001*	1.053	1.032-1.074	<0.001*
Liver cirrhosis (yes/no)	1.185	0.722-1.945	0.502			
WBC count (10 ³ /uL)	1.013	0.968-1.060	0.583			
Platelet count (10 ³ /uL)	1.000	0.996-1.003	0.851			
INR	2.334	1.866-2.920	<0.001*	2.477	1.935-3.170	<0.001*
Creatinine (mg/dL)	1.076	0.955-1.215	0.228			
Sodium (mEq/L)	1.037	0.982-1.095	0.190			
Total bilirubin (mg/dL)	1.036	1.010-1.062	0.005*	1.062	1.030-1.095	<0.001*
Albumin (g/dL)	0.814	0.511-1.297	0.387			
Ascites (yes/no)	1.522	0.909-2.548	0.110			
Hepatic encephalopathy grade III or IV (yes/no)	2.955	1.573-5.552	0.001*	1.990	1.007-3.93	0.048*

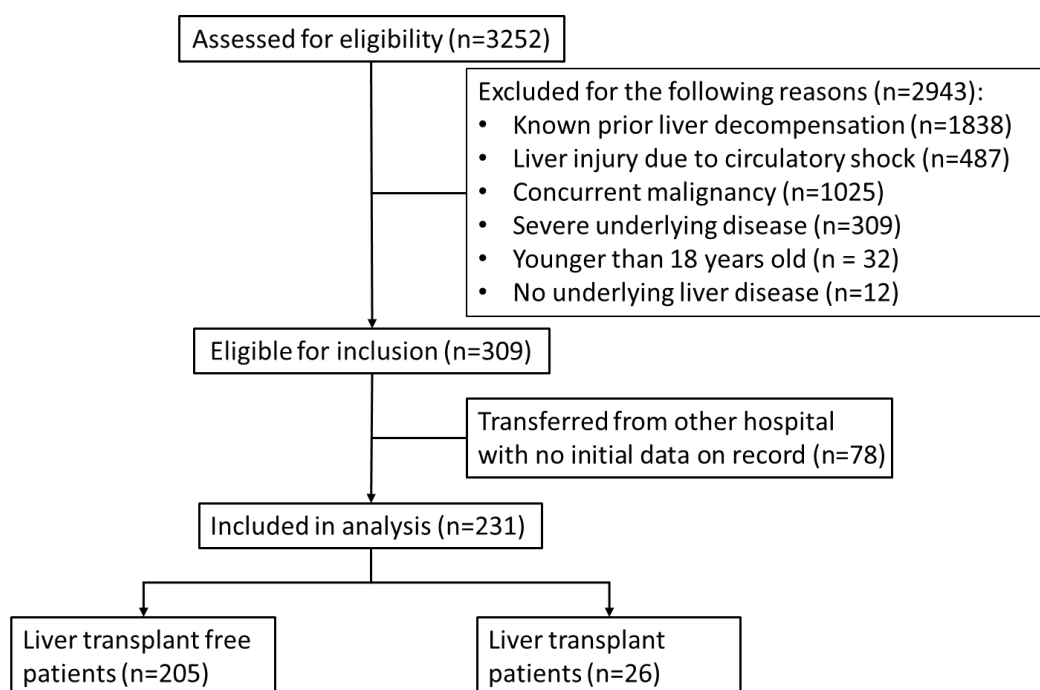


Figure 2. Relationship of CLIF-C ACLF score at Day 3-6 to cumulative mortality rate in LT-free patients with ACLF

