

Supplementary Material Online Content

eAppendix. supplementary methods

Exclusion criteria: Patients with previously recognized cirrhosis and superimposed acute on chronic liver failure were excluded. However, exceptions to the requirement of exclusion of cirrhosis were made for patients who presented with acute Wilson disease with liver failure and those with the first presentation of autoimmune-related acute liver failure (ALF). Patients not fulfilling the criteria for ALF or where primary outcomes are unknown were also excluded.

Etiology: Diagnosis codes based on the following International Classification of Diseases 9 and 10 are listed below (1) 070: Viral hepatitis; (2) 571.6, 576.1: Autoimmune liver disease (AIH, PBC, PSC); (3) 275.0: Hemochromatosis; (4) 275.1: Wilson's disease; (5) 277.6: Alpha-1-antitrypsin deficiency; (6) 453.0: Budd-Chiari syndrome; (7) 571.4: Chronic hepatitis, unspecified; (8) 571.6: Secondary or unspecified biliary cirrhosis, 571.8: Nonalcoholic fatty liver disease; (9) 303, 305.0: Alcohol use disorder; (10) 291, 357.5, 425.5, 535.3, 980.1, 980.9 somatic consequences of alcohol (except ALD); (11) 305.1-9: Drug use disorders except nicotine/caffeine; (12) 571.5: Cirrhosis, compensated; (13) 456.1, 456.21: Esophageal varices, not bleeding; (14) 456.0, 456.20: Esophageal varices, bleeding; (15) 789.5: Ascites; (16) 572.2: Hepatic encephalopathy; (17) 572.4: Hepatorenal syndrome; (18) 572.3: Portal hypertension; (19) V427: Liver transplantation status, 155.0: Hepatocellular carcinoma; (20) 155.2: Liver cancer, unspecified; (21) 572.8: Chronic or unspecified liver failure; (22) 570: Acute or subacute liver failure; and (23) 571.9: Hepatic fibrosis or sclerosis or fibrosis with sclerosis. K72: Acute and subacute hepatic failure without coma necrosis; K76.2: Central hemorrhagic necrosis of liver necrosis; K700: Alcoholic fatty liver hepatitis; K7010: Alcoholic hepatitis without ascites hepatitis; K7030: Alcoholic cirrhosis. Of liver without ascites cirrhosis. K709: Alcoholic liver disease, unspecified cirrhosis; K730: Chronic persistent hepatitis, not elsewhere classified hepatitis; K732: Chronic active hepatitis, not elsewhere classified hepatitis; K738: Other chronic hepatitis, not elsewhere classified hepatitis; K739: Chronic hepatitis,

unspecified hepatitis; K740: Hepatic fibrosis; K74.1: Hepatic sclerosis cirrhosis; K743: Primary biliary cirrhosis; K74.4: Secondary biliary cirrhosis; K74.5: Biliary cirrhosis, unspecified cirrhosis; K75.4: Autoimmune hepatitis; K76.7: Hepatorenal syndrome cirrhosis; K77: Liver disorders in diseases classified elsewhere hepatitis; K71.6: Toxic liver disease with hepatitis, not elsewhere classified hepatitis; B17.0: Acute delta-(super) infection of hepatitis B carrier hepatitis; B17.10: Acute hepatitis C without hepatic coma hepatitis; B17.2: Acute hepatitis E hepatitis; B17.8: Other specified acute viral hepatitis; B18.2: Chronic viral hepatitis C hepatitis; B18.8: Other chronic viral hepatitis; B18.9: Chronic viral hepatitis, unspecified hepatitis; B0081: Herpesviral hepatitis hepatitis; B15.0: Hepatitis A with hepatic coma hepatitis; B15.9: Hepatitis A without hepatic coma hepatitis; B16.0: Acute hepatitis B with delta-agent with hepatic coma hepatitis; B16.1: Acute hepatitis B with delta-agent without hepatic coma hepatitis; B16.2: Acute hepatitis B without delta-agent with hepatic coma hepatitis; B16.9: Acute hepatitis B without delta-agent and without hepatic coma hepatitis; B17.11: Acute hepatitis C with hepatic coma hepatitis; B17.2: Acute hepatitis E hepatitis; B17.8: Other specified acute viral hepatitis; B179: Acute viral hepatitis, unspecified hepatitis; B18.0: Chronic viral hepatitis B with delta-agent hepatitis; B18.1: Chronic viral hepatitis B without delta-agent hepatitis; B18.2: Chronic viral hepatitis C hepatitis; B19.0: Unspecified viral hepatitis with hepatic coma hepatitis; B19.10: Unspecified viral hepatitis B without hepatic coma hepatitis; B19.11: Unspecified viral hepatitis B with hepatic coma hepatitis; B19.20: Unspecified viral hepatitis C without hepatic coma hepatitis; B19.21: Unspecified viral hepatitis C with hepatic coma hepatitis; B19.9: Unspecified viral hepatitis without hepatic coma hepatitis; B25.1: Cytomegaloviral hepatitis; B25.1: Cytomegaloviral hepatitis; B26.81: Mumps hepatitis; B58.1: Toxoplasma hepatitis; B942: Sequelae of viral hepatitis; K70.11: Alcoholic hepatitis with ascites hepatitis; E83.01: Wilson's disease; K76.9: Liver disease, unspecified hepatitis; K72.90: Hepatic failure, unspecified without coma cirrhosis; K73.1: Chronic lobular hepatitis, not elsewhere classified hepatitis; K75.2: Nonspecific reactive hepatitis; B20: Human immunodeficiency virus; K75.3: Granulomatous hepatitis, not elsewhere classified

hepatitis; K75.89: Other specified inflammatory liver diseases hepatitis; K70.31: Alcoholic cirrhosis of liver with ascites cirrhosis; F10.2: Alcohol dependence; K71.7: Toxic liver disease with fibrosis and cirrhosis of the liver.

Supplementary Table 1 Unadjusted Cox proportional hazards model to predict the relationship of body mass index to Outcome in acute liver failure

Parameters	Hazard ratio	95%CI	P value
Age (years)	1.02	1.01-1.03	0.006
Gender			
Male	Ref		
Female	0.74	0.49-1.12	0.15
Ethnicity			
Hispanic	Ref		
Not Hispanic	1.17	0.43-3.19	0.76
Race			
White	Ref		
African American	0.77	0.49-1.23	0.28
Other	1.54	0.70-3.42	0.28
Unknown	0.63	0.23-1.74	0.37
Body mass index categories ¹			
Normal weight	Ref		
Overweight	2.22	1.30-3.78	0.003
Obese	2.04	1.22-3.39	0.006
Charlson comorbidity index			
0	Ref		
1-3	1.23	0.63-2.41	0.54
> 3	2.37	1.14-4.91	0.02
Etiology of acute liver failure			
Viral hepatitis	Ref		

Acetaminophen toxicity	1.35	0.56-3.21	0.51
Drug-induced liver injury	1.04	0.35-3.11	0.95
Other	3.05	1.29-7.16	0.01
Grade of hepatic encephalopathy			
I-II	Reference		
III-IV	2.83	1.78-4.50	< 0.001
Alanine aminotransferases	1.03	1.00-1.01	0.02
Aspartate aminotransferase	1.00	1.00-1.00	0.27
Alkaline phosphatase	1.00	1.00-1.00	0.83
Total bilirubin	1.01	0.99-1.02	0.39
Albumin	1.01	0.99-1.02	0.24
Prothrombin time	1.01	1.00-1.02	0.12
Activated partial thromboplastin time	1.01	1.00-1.01	0.05
International normalized ratio	1.06	0.98-1.15	0.14
Creatinine	1.09	0.99-1.19	0.07
Blood urea nitrogen	1.01	1.00-1.01	0.06
Estimated glomerular filtration rate	0.99	0.99-1.01	0.29
Total protein	1.02	1.01-1.02	0.007
Ammonia	1.00	1.00-1.01	< 0.001
Fasting glucose	1.01	1.01-1.01	0.008
Alpha-fetoprotein	0.98	0.95-1.01	0.15
Lactate	1.10	1.07-1.13	< 0.001
Phosphate	1.18	1.09-1.27	< 0.001
KCC (acetaminophen)	1.74	1.14-2.66	0.01
KCC (non-acetaminophen)	1.23	0.87-1.73	0.24
MELD	1.04	1.02-1.06	< 0.001
MELD-Na	1.04	1.02-1.06	0.001

¹Based on the World Health Organization criteria used for body mass index (BMI) categories: (1) Normal weight: BMI between 18.5 kg/m² and 24.9 kg/m²; (2)

Overweight: BMI between 25.0 kg/m² and 29.9 kg/m²; and (3) Obese: BMI $\geq$ 30 kg/m².

KCC: King's college criteria; MELD: Model for end-stage liver disease.