

Hypoxic hepatitis in cardiac intensive care unit: a study of cardiovascular risk factors, clinical course, and outcomes

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Introduction: Hypoxic hepatitis (HH) is observed frequently in intensive care units. Information in the cardiac intensive care unit (CICU) is limited. The aim of this study was to analyze the clinical course and outcomes of HH in the specific setting of the CICU.

Methods: We analyzed records of patients with HH admitted to the CICU (Group 1). Data were collected and compared with those of an intermediate group of patients with altered liver test results that did not meet the HH criteria who had a serum aminotransferase level of five to ≤ 20 times the upper-normal limit (Group 2), and with a control group who had an aminotransferase level less than five times the upper-normal limit (Group 3).

Results: Patients with HH exhibited a worse hemodynamic profile and more of these patients were in shock: 17 (94.4%) in Group 1, 14 (77.8%) in Group 2, and seven (38.9%) in Group 3 ($P=0.001$). Cardiogenic shock was the most frequent event: 12 (66.7%) in Group 1, 13 (72.2%) in Group 2, and six (33.3%) in Group 3 ($P=0.006$). The mortality rate was 55.6%. Mechanical ventilation was an independent factor associated with death (odds ratio 12.25, 95% confidence interval 1.26–118.36).

Conclusion: The mortality rate of patients with HH in CICU is high and is associated with ventilatory disturbances.

Keywords: liver dysfunction, mechanical ventilation, hospital mortality

Introduction

Hypoxia is the cornerstone of hypoxic hepatitis (HH), a state that can be caused by heart or pulmonary failure or septic shock.¹ The prevalence of HH ranges from 0.9% to 11.9%; the variation in this range can be explained by the characteristics of the clinical setting.² The low prevalence precludes identifying specific characteristics in subgroups of patients with HH. Moreover, the aminotransferase level required to make a diagnosis of HH is not clear; in some series, it is five times the upper-normal limit, and in others, it is 75 times the upper-normal limit. For this reason, there are no uniform criteria for making the diagnosis.

HH has clinical relevance because of the high in-hospital mortality of around 50%.² Various risk factors associated with the high mortality rate in HH patients have been postulated: high levels of serum aspartate aminotransferase (AST), lactate dehydrogenase, or lactate; the International Normalized Ratio; and the presence of septic shock.³ Renal replacement therapy and use of vasopressor therapy have also been reported as mortality risk factors.⁴

There is little information about the specific settings associated with HH, such as the cardiac intensive care unit (CICU). Some differences have been reported. For

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example, HH patients present with high central venous pressure (CVP) and low hepatic blood flow.⁵ More recent data show that patients with an acute myocardial lesion have an elevated aminotransferase level, which correlates with right cardiac dysfunction and elevated hepatic venous pressure.⁶ The specific characteristics of this setting suggest that HH may follow different courses, but information is scarce.

The primary aim of this study was to analyze the clinical course and outcomes of HH in the specific setting of a cardiac intensive care unit. The secondary aim was to compare these variables between patients without HH but with significantly altered liver function and HH patients treated in a cardiac intensive care unit.

Materials and methods

A retrospective case-control study was performed in the cardiac intensive care unit of the Medica Sur Clinic and Foundation university hospital from 2008 to 2011. Three groups of patients were included in the study. Group 1 comprised patients diagnosed with HH with a serum aminotransferase level >20 times the upper-normal limit within the clinical context of cardiac arrest, shock, or acute heart failure. Group 2 included patients with a significant alteration in liver function, defined as a serum aminotransferase level of five to ≤ 20 times the upper-normal limit (Group 2). Group 3 comprised a control group of patients with an aminotransferase level less than five times the upper-normal limit (Group 3). The patients with significantly altered liver function and the control group were hospitalized in the same cardiac intensive care unit and were matched for sex and age. The exclusion criteria included infection with hepatitis virus, use of drugs with demonstrated hepatotoxicity, or abdominal trauma.

Demographic and clinical information were extracted from paper-based and electronic files. The diagnosis at admission to the cardiac intensive care unit, characteristics of shock, and use of vasopressors were recorded. The results of the liver function tests (levels of AST, alanine aminotransferase, total bilirubin, direct bilirubin, alkaline phosphatase, and gamma-glutamyl transpeptidase) were recorded at baseline, and the highest values reported during hospitalization in the cardiac intensive care unit were recorded.

Hemodynamic status was analyzed through the following variables: mean blood pressure; CVP; cardiac output; cardiac index; systemic vascular resistance index; systolic volume; and systolic volume index.⁷

Myocardial function was analyzed by echography and the following data were recorded: left ventricular ejection frac-

tion calculated by Simpson's rule and the Teichholz formula; fractional area shortening; left and right ventricular myocardial performance indexes; lateral and medial mitral annular tissue Doppler velocities; pulsed-wave tissue Doppler velocity of the tricuspid annular plane systolic excursion (TAPSE); mean pulmonary artery pressure; right ventricular ejection fraction; tissue Doppler E/E' ratio; and cardiac output.⁸ Serum B-type natriuretic peptide concentration was also measured as a marker of heart failure.⁹

Ventilation was assessed by measuring arterial blood gases: carbon dioxide arterial pressure; oxygen arterial pressure; oxygen saturation; lactate concentration; Kirby index; arteriovenous shunt; and alveolar-arterial O₂ gradient.¹⁰

Renal dysfunction was defined as high blood urea nitrogen or serum creatinine concentration, or the need for therapy (peritoneal dialysis or hemodialysis).¹¹

The study was approved by the Human Subjects Committee of the Medica Sur Clinic and Foundation as conforming to the ethical guidelines of the 1975 Declaration of Helsinki. Consent was obtained from all patients to analyze their data for research. All participants signed a written informed consent to allow the use of their data for research purposes.

Statistical analysis

The variables are described by measures of central tendency and dispersion. Continuous variables were compared using analysis of variance and the Bonferroni post hoc test for multiple comparisons. Categorical data were compared using Fisher's exact test or the χ^2 test. To identify risk factors associated with mortality, multivariate unconditional logistic regression analyses were conducted. Multicollinearity in the adjusted models was tested by deriving a covariance matrix. To discriminate those factors associated with mortality, the area under the curve was calculated. A P -value <0.05 was considered significant. All statistical analyses were conducted using the statistics program SPSS/PC version 12.0 (IBM Corporation, Armonk, NY, USA).

Results

During the analyzed period, 1,649 patients were admitted to the cardiac intensive care unit. Eighteen cases of HH were identified, with a prevalence of 1.09%. There were no differences between the groups in demographics, diagnosis, and morbid conditions (Table 1). Most patients with HH developed shock, defined as a mean arterial pressure <65 mmHg, lack of response to fluid resuscitation, and the need for vasopressors to maintain mean arterial pressure above this value. Seventeen (94.4%) patients in Group 1, 14 (77.8%) patients

Table 1 Demographic and clinical characteristics of patients in the cardiac intensive care unit

	Group 1 (n=18)	Group 2 (n=18)	Group 3 (n=18)	P-value
Male n (%)	12 (66.7%)	12 (66.7%)	12 (66.7%)	1
Age (years)	61±17	61±17	60±17	0.998
Body mass index (kg/m ²)	27±5	29±6	27±6	0.374
Diabetes mellitus n (%)	5 (27.8%)	4 (22.2%)	7 (38.9%)	0.53
High blood pressure n (%)	7 (38.9%)	11 (61.1%)	8 (44.4%)	0.38
Heart failure n (%)	0	1 (5.6%)	1 (5.6%)	0.59
Cardiovascular disease n (%)	5 (27.8%)	7 (38.9%)	6 (33.3%)	0.77
Chronic liver disease n (%)	2 (11.1%)	0	1 (5.6%)	0.34
Chronic lung disease n (%)	1 (5.6%)	2 (11.1%)	1 (5.6%)	0.76
Chronic kidney disease n (%)	1 (5.6%)	3 (16.7%)	3 (16.7%)	0.51
Diagnosis				
Myocardial infarction n (%)	8 (44.4%)	11 (61.1%)	7 (38.9%)	0.308
Cardiac arrhythmia n (%)	3 (16.8%)	1 (5.6%)	1 (5.6%)	
Acute aortic syndrome n (%)	1 (5.6%)	0	3 (16.7%)	
Acute heart failure n (%)	0	3 (16.7%)	1 (5.6%)	
Pulmonary embolism n (%)	2 (11.1%)	1 (5.6%)	1 (5.6%)	
Tamponade n (%)	3 (16.7%)	0	1 (5.6%)	
Hospital stay (days)	8±5	8±5	8±6	0.990
Intensive care unit stay (days)	4±2	5±3	4±4	0.470
Mortality n (%)	10 (55.6%)	6 (35.3%)	2 (11.1%)	0.019

Note: Data are expressed as mean ± standard deviation or n (%).

in Group 2, and seven (38.9%) patients in Group 3 ($P=0.001$) developed shock (Table 2). The most common cause of shock was cardiogenic shock, defined as a systolic blood pressure of <90 mmHg for >30 minutes secondary to myocardial dysfunction, cardiac index <2.2 L/min/m², or pulmonary capillary wedge pressure >15 mmHg. Cardiogenic shock

was less common in Group 3; 12 (66.7%) patients in Group 1, 13 (72.2%) patients in Group 2, and six (33.3%) patients in Group 3 ($P=0.006$) developed cardiogenic shock. The use of vasoactive drugs differed between the groups, particularly for norepinephrine (16 [88.9%] patients in Group 1, 14 [77.8%] patients in Group 2, and seven [38.9%] patients in

Table 2 Hemodynamic status, hemodynamic drugs, and echocardiographic parameters

	Total (n=54)	Group 1 (n=18)	Group 2 (n=18)	Group 3 (n=18)	P-value
Shock	38 (70.4)	17 (94.4)	14 (77.8)	7 (38.9)	0.001
Cardiogenic shock	31 (57.4)	12 (66.7)	13 (72.2)	6 (33.3)	
Septic shock	3 (5.6)	2 (11.1)	1 (5.6)	0	0.006
Mixed shock	4 (7.4)	3 (16.7)	0	1 (5.6)	
Dopamine	19 (35.2)	8 (44.4)	6 (33.3)	5 (27.8)	0.566
Norepinephrine	37 (68.5)	16 (88.9)	14 (77.8)	7 (38.9)	0.003
Vasopressin	27 (50)	12 (66.7)	10 (55.6)	5 (27.8)	0.056
Epinephrine	9 (16.7)	3 (16.7)	5 (27.8)	1 (5.6)	0.202
Levosimendan	33 (61.1)	13 (72.2)	13 (72.2)	7 (38.9)	0.060
Phenylephrine	11 (20.4)	8 (44.4)	2 (11.1)	1 (5.6)	0.007
Dobutamine	4 (7.4)	1 (5.6)	1 (5.6)	2 (11.1)	0.763
Intra-aortic balloon pump	10 (18.5)	4 (22.2)	4 (22.2)	2 (11.1)	0.612
CVP lowest (cmH ₂ O) ^a		8±5*	6±5	2±5	0.006
CO lowest (L/min) ^a		4.1±2.1	3.5±1.8	4.9±2.3	0.704
MAP lowest (mmHg)		54±15	58±14	59±14	0.602
SAP lowest (mmHg)		73±25	83±15	87±20	0.112
CI lowest (L/min/m ²) ^a		2.3±1.1	1.6±0.9	2.7±1.2	0.429
TAPSE (mm)		15±6*	18±4	22±6	0.035
EF LV by Teichholz formula (%) ^a		52±18	56	59±21	0.863
EF LV by Simpson's rule (%) ^a		41±15	45±11	53±15	0.058

Notes: Data are expressed as mean ± standard deviation or n (%). * $P<0.05$ versus Group 3.

Abbreviations: CI, cardiac index; CO, cardiac output; CVP, central venous pressure; EF, ejection fraction; LV, left ventricle; MAP, mean arterial pressure; SAP, systolic arterial pressure; TAPSE, tricuspid annular plane systolic excursion.

Group 3; $P=0.003$) and phenylephrine (eight [44.4%] patients in Group 1, two [11.1%] patients in Group 2, and one [5.6%] patient in Group 3; $P=0.007$).

The levels of transaminases, lactate dehydrogenase, and bilirubin differed between Groups 1 and 2, and between Groups 1 and 3, but not between Groups 2 and 3 (Table 3).

Hemodynamic variables such as mean arterial pressure, cardiac output, systemic vascular resistance index, systolic volume, and systemic vascular resistance were lower in Group 1 but did not differ between Groups 2 and 3, except for CVP, which was significantly higher in Group 1 compared with Group 3 (8 ± 5 cmH₂O in Group 1, 6 ± 5 cmH₂O in Group 2, and 2 ± 5 cmH₂O in Group 3; $P<0.05$) (Table 2). The echocardiographic variables showed a trend toward different left ventricular function between groups. In the assessment of right ventricular function, TAPSE differed significantly between Groups 1 and 3 (15 ± 6 versus 22 ± 6 mm; $P=0.035$).

Evaluation of ventilatory function produced results for only 17 patients in Group 1, 15 in Group 2, and 13 in Group 3 (Table 4). The requirement for ventilatory support was higher in Group 1, which showed worse ventilatory function with shunts ($39\%\pm 16\%$ in Group 1, $25\%\pm 11\%$ in Group 2, and $27\%\pm 12\%$ in Group 3; $P=0.004$), oxygen saturation ($82\%\pm 16\%$ in Group 1, $93\%\pm 6\%$ in Group 2, and $90\%\pm 8\%$ in Group 3; $P=0.026$), and Kirby index (93 ± 73 mmHg in Group 1, 167 ± 88 mmHg in Group 2, and 125 ± 82 mmHg in Group 3; $P=0.046$). Serum lactate concentration was higher in patients with HH or with altered liver function (8.8 ± 6.6 mmol/L in Group 1, 6.6 ± 4.3 mmol/L in Group 2, and 2.7 ± 1.9 mmol/L in Group 3; $P=0.005$). The lowest PaO₂ values were 67 ± 27 mmHg, 118 ± 84 mmHg, and 63 ± 14 mmHg in Groups 1, 2, and 3, respectively; Group 2 differed significantly from the other two groups ($P=0.009$).

None of the measures of renal function or the use of replacement therapy with dialysis differed between the groups (Table 5).

The length of stay in the cardiac intensive care unit and hospital did not differ between groups (Table 1). Eighteen patients died during their stay. Most patients who died had HH; 10 (55.6%) died in Group 1, six (35.3%) died in Group 2, and two (11.1%) died in Group 3. Factors related to mortality were preexistent chronic liver disease, shock, cardiogenic shock, use of norepinephrine, use of vasopressors, use of an intra-aortic balloon pump, and mechanical ventilation (Table 6). However, in multivariate analysis, only mechanical ventilation was associated with an increased risk of death (odds ratio 12.25, 95% confidence interval 1.26–118.36; $P<0.001$). We determined the area under the curve to assess the ventilation variables and found that having a higher arteriovenous shunt was a significant variable associated with death (area under the curve 0.721, 95% confidence interval 0.563–0.879).

Discussion

HH is a common condition in critically ill patients. The prevalence is around 1 in 1,000 hospital admissions and can be ten times higher in the intensive care unit. Its prevalence is unknown in other critical care settings such as the cardiac intensive care unit, and there is only one study in the literature related to other critical care settings.⁵ The current study adds new information about a condition in a setting with limited information.

Heart failure, respiratory failure, and septic shock account for >90% of all HH cases. Several hemodynamic mechanisms are involved in liver hypoxia.² Heart failure from various etiologies is the main underlying condition in HH, but HH

Table 3 Baseline and maximum levels of aspartate aminotransferase, alanine aminotransferase, and lactic dehydrogenase

	Group 1 (n=18)	Group 2 (n=18)	Group 3 (n=18)	P-value
Baseline AST (U/L)	1,521 $\pm$ 2,320*** 451 (35–9,597)	260 $\pm$ 185 281 (25–670)	55 $\pm$ 49 36 (14–192)	0.004
AST max (U/L)	3,275 $\pm$ 3,001*** 2,205.5 (1,077–12,261)	394 $\pm$ 122 376.5 (236–670)	60 $\pm$ 49 43.5 (14–192)	0.001
Baseline ALT (U/L)	810 $\pm$ 954*** 389.5 (19–3,215)	159 $\pm$ 131 106 (12–384)	43 $\pm$ 45 29 (9–197)	0.0001
ALT max (U/L)	1,736 $\pm$ 1,378*** 1,394 (502–6,243)	227 $\pm$ 132 236 (58–443)	44 $\pm$ 44 29 (9–197)	0.001
Baseline LDH (U/L)	2,058 $\pm$ 2,398*** 1,057 (255–5,264)	541 $\pm$ 355 403.5 (175–1,301)	249 $\pm$ 131 230.5 (93–576)	0.001
LDH max (U/L)	4,425 $\pm$ 3,199*** 3,862 (1,544–14,679)	831 $\pm$ 310 864.5 (564–1,408)	266 $\pm$ 141 241.5 (111–576)	0.001

Notes: Data are expressed as mean $\pm$ standard deviation or median (minimum–maximum). * $P<0.05$ versus Group 2; ** $P<0.05$ versus Group 3.

Abbreviations: AST, aspartate aminotransferase; ALT, alanine aminotransferase; LDH, lactic dehydrogenase.

Table 4 Evaluation of ventilatory function by group

	Group 1 (n=17)	Group 2 (n=15)	Group 3 (n=13)	P-value
PaCO ₂ higher (mmHg)	41±14	37±10	39±6	0.575
PaO ₂ lower (mmHg)	67±27	118±84***	63±14	0.009
SaO ₂ lower (%)	82±16*	93±6	90±8	0.026
Serum lactate higher (mmol/L)	8.8±6.6**	6.6±4.3	2.7±1.9	0.005
Kirby Index lower (mmHg)	93±73*	167±88	125±82	0.046
O ₂ A-a gradient (mmHg)	368±133*	282±153	309±166	0.264
Shunts higher (%)	39±16	25±11	27±12	0.014
Mechanical ventilation	12 (70.6)	11 (61.1)	5 (27.8)	0.028

Notes: Data are expressed as mean ± standard deviation or n (%). *P<0.05 versus Group 2; **P<0.05 versus Group 3; ***P<0.05 versus Group 3.

Abbreviations: A-a, alveolar-arterial; O₂, oxygen; PaCO₂, carbon dioxide arterial pressure; PaO₂, oxygen arterial pressure; SaO₂, oxygen saturation.

is also detected in association with other cardiac conditions such as acute myocardial infarction, pulmonary embolism, and cardiac tamponade. In patients admitted for cardiogenic shock, the severity of hypotension and a decrease in cardiac output can be related to the development of HH.² However, the incidence of cardiogenic shock and its correlation with HH have not been defined. In the current study, we found that hemodynamic instability characterized the group of patients who developed HH. Their main features were lower mean arterial pressure, systolic pressure, and vascular resistance.

Shock is one of the most frequent conditions associated with the development of HH, and septic shock is involved most often.^{2,3} This association was confirmed in the present study; however, because our study was performed in a cardiac intensive care unit, we found that cardiogenic shock was the predominant type of shock involved.

The use of vasopressors is associated with the development of HH, which may result from hypoxia reperfusion with deleterious effects on hepatic blood flow.⁴ In our study, phenylephrine and norepinephrine were related to the development of HH, confirming this relationship. Another hemodynamic factor crucial to the pathophysiological mechanisms of HH is passive congestion of the liver secondary to right heart failure.⁵ This was confirmed in our study by the significantly higher CVP and lower TAPSE score in the

HH group compared with the other groups. This may reflect right ventricular overload and impaired function. We note that other values, such as the myocardial performance index, better reflect the overall performance of the right ventricle; however, TAPSE is the most cited variable for the evaluation of right ventricular function.¹²

Respiratory failure is the second most frequent cause of HH and is responsible for 7%–15% of cases.^{2,13} Hypoxia is the main hemodynamic factor in the development of HH in respiratory failure. We found that patients with HH had a greater need for mechanical ventilation (61.1% compared with 27.8% in the control group) and worse oxygenation parameters such as lower PaO₂, SaO₂, and increased shunts. All of these variables support the idea that respiratory failure is associated with HH when coupled with an environment of heart disease.

Two prior studies^{2,4} described acute kidney failure as an aid in diagnosing patients with HH because acute kidney failure is an outcome of hemodynamic disturbances that characterize this set of patients, and its presence is unusual in viral or drug-induced hepatitis. One study reported kidney failure to be an independent risk factor for mortality.¹⁴ In our study, kidney failure and renal replacement therapy were not associated with the development of HH or with mortality. However, the previous series^{2,4} included patients in worse clinical condition than those in our study.

Table 5 Evaluation of renal function by group

	Group 1 (n=18)	Group 2 (n=18)	Group 3 (n=18)	P-value
Baseline blood urea nitrogen (mg/dL)	37±27 27.4 (11.5–108.6)	24±14 17.9 (9.7–45.5)	35±47 17.75 (10.6–214.4)	0.420
Highest blood urea nitrogen (mg/dL)	41±26 30.55 (14–108.6)	28±18 22.6 (9.7–70.5)	48±52 24.4 (10.6–214.4)	0.221
Baseline creatinine (mg/dL)	2.9±4.9 1.22 (0.8–21.76)	1.4±0.9 1.19 (0.66–4.52)	1.9±2.6 1.175 (0.64–12.32)	0.412
Highest creatinine (mg/dL)	2.9±4.8 1.45 (0.8–21.7)	1.7±1.3 1.3 (0.78–6.28)	2.4±2.9 1.19 (0.72–12.32)	0.522
Dialysis n (%)	4 (22.2)	2 (11.8)	3 (17.6)	0.715

Note: Data expressed as mean ± standard deviation, median (minimum–maximum), or n (%).

Table 6 Clinical features according to mortality

Clinical feature	Survived (n=36)	Died (n=18)	P-value
Shock state	20 (55.6)	18 (100)	0.001
Cardiogenic shock	16 (44.4)	15 (83.3)	
Septic shock	2 (5.6)	1 (5.6)	0.009
Mixed shock	2 (5.6)	2 (11.1)	
Use of dopamine	11 (30.6)	8 (44.4)	0.239
Use of norepinephrine	20 (55.6)	17 (94.4)	0.003
Use of vasopressin	12 (33.3)	15 (83.3)	0.001
Use of adrenaline	3 (8.3)	6 (33.3)	0.029
Use of levosimendan	20 (55.6)	13 (72.2)	0.188
Use of phenylephrine	4 (11.1)	7 (38.9)	0.023
Use of dobutamine	4 (11.1)	0	0.186
Use of intra-aortic balloon pump	1 (2.8)	9 (50)	0.001
Mechanical ventilation	13 (36.1)	15 (88.2)	0.001
Dialysis	4 (11.8)	5 (27.8)	0.143

Note: Data are expressed as n (%).

The prognosis of HH is poor, and more than half of patients will die during their stay in, or shortly after their discharge from the intensive care unit. The five largest series on HH reported mortality rates ranging from 45% to 72%.² The mortality rate was 56% in our study, a rate that is within this range. The factors associated with increased mortality in HH patients were preexisting liver disease, cardiogenic or septic shock, use of vasopressors (vasopressin, epinephrine, or norepinephrine), and the need for mechanical ventilation. All of these reflect circulatory collapse and respiratory failure. None of the diagnoses at baseline were related to mortality. Acute coronary syndrome in association with heart failure^{4,7} was the most common diagnosis in our series, but it was not related to the incidence of, or mortality from, HH. Other important outcomes measured were days of hospital stay and days within the cardiac intensive care unit, which did not differ between groups.

Henrion et al⁵ studied high-risk patients in a cardiac intensive care unit and reported a prevalence of 2.6% in 766 patients; 21.9% of these patients exhibited low cardiac output, which was double the percentage found in our series. They compared hepatic blood flow by galactose clearance and hemodynamic variables between patients with low cardiac output and HH and those with low cardiac output without HH. HH was frequent in patients with low cardiac output admitted to the cardiac intensive care unit. In our study, we included all patients admitted to the cardiac intensive care unit, not only high-risk patients. We also found a higher CVP in the HH group. Hepatic flow was not measured directly, but we obtained an indirect indication of right heart failure, which reflects passive hepatic venous congestion, by measuring TAPSE, which was lower in patients who developed HH.

Our study is the first to include an intermediate group of patients (Group 2) with altered liver function who do not meet the criteria for HH. This particular group had more cardiogenic shock events than the HH group, although the difference was not significant. Group 2 also showed a worse hemodynamic profile, with lower cardiac index and cardiac output. There was a slight tendency toward increased mortality in patients who met the HH criteria, being high (35.3%). Thus, it is important to pay attention to patients with cardiogenic shock who do not meet all the HH criteria. More research is needed on this forgotten group of patients.

Limitation of the study

First, the present study had a retrospective design, and limited information could be obtained. However, our results are similar to those of the only prospective study on this topic.⁸ Second, our sample was small, and this may have affected our ability to detect some relationships between outcomes such as an association with kidney failure, which has been reported in other studies.^{2,4} Third, we did not use a direct method to measure hepatic blood flow.

Conclusion

In conclusion, HH is an uncommon condition in patients admitted to the cardiac intensive care unit, but it has a high mortality rate. Cardiogenic shock is an important cause of HH. Mechanical ventilation and the use of vasopressors are independent risk factors for the development of HH. Patients with abnormal liver function who do not meet the criteria for HH may have an unclear prognosis, and further research is needed to clarify the clinical course in this group of patients.

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Author contributions

OGC developed the idea for this study. NCCT developed the idea for this study, performed literature search, analyzed data, and wrote the manuscript. PMM, BVVG, MHG, and SGL collaborated to design the protocol, performed literature search, analyzed data, and reviewed and edited the manuscript. MU reviewed the manuscript. All authors have approved the final version of this article, including the authorship list.

Disclosure

The authors report no conflicts of interest in this work.

Key messages

- Cardiogenic shock was the predominant type of shock involved with the development of HH in cardiac intensive care unit.
- Mechanical ventilation is an independent risk factor to the development of HH.
- Those patients with altered liver function tests who do not meet criteria for HH should be followed carefully.

References

1. Henrion J, Schapira M, Luwaert R, Colin L, Delannoy A, Heller FR. Hypoxic hepatitis: clinical and hemodynamic study in 142 consecutive cases. *Medicine (Baltimore)*. 2003;82(6):392–406.
2. Henrion J. Hypoxic hepatitis. *Liver Int*. 2012;32(7):1039–1052.
3. Fuhrmann V, Kneidinger N, Herkner H, et al. Hypoxic hepatitis: underlying conditions and risk factors for mortality in critically ill patients. *Intensive Care Med*. 2009;35(8):1397–1405.
4. Fuhrmann V, Kneidinger N, Herkner H, et al. Impact of hypoxic hepatitis on mortality in the intensive care unit. *Intensive Care Med*. 2011;37(8):1302–1310.
5. Henrion J, Descamps O, Luwaert R, Schapira M, Parfonry A, Heller F. Hypoxic hepatitis in patients with cardiac failure: incidence in a coronary care unit and measurement of hepatic blood flow. *J Hepatol*. 1994;21(5):696–703.
6. Myers RP, Cerini R, Sayegh R, et al. Cardiac hepatopathy: clinical, hemodynamic, and histologic characteristics and correlations. *Hepatology*. 2003;37(2):393–400.
7. Pinsky MR. Functional hemodynamic monitoring. *Intensive Care Med*. 2002;28(4):386–388.
8. Vignon P. Hemodynamic assessment of critically ill patients using echocardiography Doppler. *Curr Opin Crit Care*. 2005;11(3):227–234.
9. McCullough PA, Nowak RM, McCord J, et al. B-type natriuretic peptide and clinical judgment in emergency diagnosis of heart failure: analysis from Breathing Not Properly (BNP) Multinational Study. *Circulation*. 2002;106(4):416–422.
10. Shneerson JM. Techniques in mechanical ventilation: principles and practice. *Thorax*. 1996;51(7):756–761.
11. Bailie GR, Uhlig K, Levey AS. Clinical practice guidelines in nephrology: evaluation, classification, and stratification of chronic kidney disease. *Pharmacotherapy*. 2005;25(4):491–502.
12. Burgess MI, Bright-Thomas RJ, Ray SG. Echocardiographic evaluation of right ventricular function. *Eur J Echocardiogr*. 2002;3(4):252–262.
13. Raurich JM, Llompert-Pou JA, Ferreruela M, et al. Hypoxic hepatitis in critically ill patients: incidence, etiology and risk factors for mortality. *J Anesth*. 2011;25(1):50–56.
14. Raurich JM, Pérez O, Llompert-Pou JA, Ibáñez J, Ayestarán I, Pérez-Bárcena J. Incidence and outcome of ischemic hepatitis complicating septic shock. *Hepatol Res*. 2009;39(7):700–705.

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