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Prognostic value of elevated transaminase levels as predictors of adverse outcomes in patients with acute myocardial infarction

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ABSTRACT

Aim. To assess the prevalence of elevated serum liver transaminases (LTs), including alanine aminotransferase (ALT) and aspartate aminotransferase (AST), and their impact on in-hospital and long-term mortality in patients with acute myocardial infarction (AMI).

Materials and methods. The prospective observational study included 416 consecutive AMI patients (median age 65 years, 40.9% female, 46.9% with ST elevation) without prior liver diseases, who underwent coronary angiography within 24 hours after hospitalization. AST and ALT levels were measured upon admission. LTs were considered as abnormal when their levels exceeded the local upper limit of normal. Clinical endpoints were all-cause in-hospital and 18-month mortality. Associations between clinical endpoints and various risk factors, including LT levels, were assessed by the multivariate logistic regression analysis.

Results. Elevated LT levels were seen in 28.6% of AMI patients: an isolated increase in ALT was noted in 17.8% of patients, while an isolated increase in AST was registered in 25% of cases. In-hospital and 18-month mortality was 5.8 and 11.3%, respectively. Abnormal LT levels were associated with the presence of ST elevation (odds ratio (OR) 1.873, 95% confidence interval (CI) 1.218–2.881, $p = 0.004$), lower systolic and diastolic blood pressure (OR 0.993, 95% CI 0.986–1.0, $p = 0.04$ and 0.979, 95% CI 0.964–0.994, $p = 0.007$, respectively), higher Killip class (OR 1.510, 95% CI 1.142–1.999, $p = 0.004$), and higher creatinine level (OR 1.010, 95% CI 1.003–1.016, $p = 0.004$). In the multivariate analysis, elevated LT levels were independently associated with in-hospital and 18-month mortality (OR 3.607, 95% CI 1.199–10.848, $p = 0.022$ and 2.182, 95% CI 1.011–4.708, $p = 0.047$, respectively).

Conclusion. Elevated LT levels were present in about a third of patients with AMI. They were associated with specific clinical, biological, and prognostic features, including in-hospital and long-term mortality in AMI patients.

Keywords: acute myocardial infarction; alanine transaminase; aspartate transaminase; in-hospital mortality; long-term mortality, prognosis

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Прогностическая ценность повышенного уровня трансаминаз в качестве предиктора неблагоприятного исхода у больных с острым инфарктом миокарда

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РЕЗЮМЕ

Цель. Оценить распространенность повышенного уровня аланинаминотрансферазы (аланинтрансаминазы, АЛТ) и аспартатаминотрансферазы (аспартаттрансаминазы, АСТ) у больных с острым инфарктом миокарда (ОИМ) и их возможное прогностическое влияние на госпитальную и долгосрочную смертность.

Материалы и методы. Проспективное наблюдательное исследование включало 416 последовательных пациентов с ОИМ без известного на момент госпитализации заболевания печени (медиана возраста 65 лет, 40,9% женщин, 46,9% с подъемом сегмента ST), которым выполняли коронарографию в течение первых 24 ч после поступления в стационар. Сывороточные показатели АСТ и АЛТ определялись сразу при поступлении. Значения сывороточных трансаминаз считались повышенными, если их уровень превышал верхнюю границу нормы, определенной для локальной лаборатории. Конечными клиническими точками обсервационного исследования были определены внутрибольничная и 18-месячная смертность. Связь между клиническими конечными точками и вероятными факторами риска, включая уровень сывороточных трансаминаз, оценивались с применением многофакторного логистического регрессионного анализа.

Результаты. Повышенные значения трансаминаз наблюдались у 28,6% пациентов с ОИМ: изолированное повышение АЛТ отмечалось у 17,8% больных, изолированная гиперферментемия АСТ – в 25% случаев. Внутрибольничная и 18-месячная смертность в исследовании составили 5,8 и 11,3% соответственно. Повышение уровня трансаминаз было связано с регистрацией подъема сегмента ST на электрокардиограмме (отношение шансов (ОШ) 1,873; 95%-й доверительный интервал (ДИ) 1,218–2,881; p = 0,004), более низким систолическим и диастолическим артериальным давлением (ОШ 0,993; 95%-й ДИ 0,986–1,0; p = 0,04 и 0,979; 95%-й ДИ 0,964–0,994; p = 0,007 соответственно), высоким классом острой сердечной недостаточности по шкале Killip (ОШ 1,510; 95%-й ДИ 1,142–1,999; p = 0,004) и повышением уровня креатинина (ОШ 1,010; 95%-й ДИ 1,003–1,016; p = 0,004). В многофакторном анализе повышение трансаминаз независимо было ассоциировано с внутрибольничной и 18-месячной смертностью (ОШ 3,607; 95%-й ДИ 1,199–10,848; p = 0,022 и 2,182; 95%-й ДИ 1,011–4,708; p = 0,047 соответственно).

Заключение. Повышенный уровень трансаминаз обнаружен у трети пациентов с ОИМ. Он ассоциирован с определенными клиническими, биологическими и прогностическими особенностями, включая отрицательное прогностическое влияние на внутрибольничную и долгосрочную смертность пациентов с ОИМ.

Ключевые слова: аланинтрансаминаза, аспартаттрансаминаза, внутрибольничная смертность, долгосрочная смертность, острый инфаркт миокарда, прогноз

Конфликт интересов. Авторы заявляют об отсутствии явного или потенциального конфликта интересов, связанного с публикацией данной статьи.

Источник финансирования. Авторы объявляют об отсутствии финансирования при проведении исследования.

Соответствие принципам этики. Все участники подписали информированное согласие на участие в исследовании. Исследование одобрено этическим комитетом Российского университета дружбы народов им. Патриса Лумумбы.

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INTRODUCTION

Acute myocardial infarction (AMI) is a critical manifestation of coronary artery disease (CAD), characterized by obstruction of coronary artery, leading to myocardial ischemia and subsequent necrosis of myocardial tissue [1]. AMI causes acute heart failure, resulting in reduction of cardiac output, tissue perfusion, and passive venous congestion [2]. These hemodynamic alterations significantly affect the liver, which receives about one-quarter of the total cardiac output [3]metabolism, clearance, and host defense are tightly dependent on an adequate microcirculation. To guarantee hepatic homeostasis, this requires not only a sufficient nutritive perfusion and oxygen supply, but also a balanced vasomotor control and an appropriate cell-cell communication. Deteriorations of the hepatic homeostasis, as observed in ischemia/reperfusion, cold preservation and transplantation, septic organ failure, and hepatic resection-induced hyperperfusion, are associated with a high morbidity and mortality. During the last two decades, experimental studies have demonstrated that microcirculatory disorders are determinants for organ failure in these disease states. Disorders include 1.

In clinical practice, serum levels of alanine transaminase (ALT) and aspartate transaminase (AST) are routinely assessed to evaluate liver function [4]. ALT, primarily localized in hepatocytes with minimal distribution in cardiac, renal, and muscular tissues, serves as a specific marker for hepatic dysfunction [4]. In contrast, AST is derived not only from hepatic tissue but also from various other tissues, including the heart, erythrocytes, skeletal muscles, kidney, and brain. Elevated AST levels are observed following ischemic cell death in these tissues [4]. While previous studies have demonstrated an association between abnormal transaminase levels and cardiovascular outcomes [5–8]as a proxy marker of NAFLD, and death from cardiovascular disease (CVD, the prevalence of elevated transaminase levels and related outcomes in patients with AMI remain understudied.

The aim of the study was to assess the prevalence of elevated serum liver transaminases and factors associated with them in a cohort of AMI patients and to evaluate their impact on in-hospital and long-term all-cause mortality.

MATERIALS AND METHODS

A single-center, prospective, observational study was conducted in the Vinogradov Municipal Clinical Hospital (Moscow, Russia) from January 2021 to December 2022. The study included patients aged >18 years presenting with AMI who underwent coronary angiography < 24 hours from symptom onset. The exclusion criteria were: patients diagnosed with type 3, 4, and 5 myocardial infarction (MI), as well as those who developed MI during hospitalization. Additionally, individuals with elevated liver transaminases (LTs) indicative of hepatitis B or C, cirrhosis of the liver, fatty liver disease, hepatobiliary obstructive disease, bone disease, pancreatitis, infectious diseases or individuals after a known episode of alcohol consumption prior to the index event (the AST / ALT ratio of more than 2) were excluded from the study [9]. The AMI diagnosis was established following the Third Universal Definition of MI [10].

We collected baseline demographic and clinical characteristics, cardiovascular risk factors, comorbidities, physical examination data, as well as blood test and imaging findings (including electrocardiography, echocardiography, and

coronary angiography). Patients with incomplete medical history were excluded from the dataset. All blood samples obtained upon admission were analyzed in the core laboratory of Vinogradov Municipal Clinical Hospital.

Cardiac troponin I levels were measured using the Access 2 Immunoassay System (Beckman Coulter, USA) with a 99th-percentile upper reference limit of 0.02 ng / l. LTs were measured using the Beckman Coulter Clinical Chemistry Analyzer (AU 680) and considered abnormal when the levels exceeded 50 U / l for ALT and 50 U / l for AST. Furthermore, liver injury was classified according to the extent of liver enzyme elevation: mild (1–2 times higher than the upper limit of normal (ULN)), moderate (≥ 2–5 times higher than the ULN), and severe (≥ 5 times higher than the ULN) [11, 12]. Risk stratification of MI patients was assessed using the GRACE (Global Registry of Acute Coronary Events) 2.0 score [13].

The primary endpoint was in-hospital mortality, which was obtained from medical records. The secondary endpoint was 18-month mortality. Mortality was defined as all-cause death that was recorded in patient medical records and death registers. Long-term mortality was evaluated using structured telephone interviews at 1, 3, 6, 12, 15, and 18 months after discharge. At the study closing date, all follow-up information was available. The study complied with the principles of the Declaration of Helsinki and was approved by the local Ethics Committee at the Institute of Medicine, RUDN University. All patients signed an informed consent to participate in the study.

Statistical analysis

Statistical analysis was performed using the IBM SPSS Statistics 25.0 software package (SPSS Inc., Chicago, IL, USA). Categorical variables were described as frequencies and percentages, while continuous variables were presented as the median and the interquartile range (*Me* (Q_1; Q_3)). The Chi-square test or the Fisher's exact test was used to compare categorical variables, and the Kruskal – Wallis test was used for to compare continuous variables between the groups. The univariate and multivariate logistic regression models were used to identify risk factors associated with elevated LTs in AMI patients, as well as factors associated with in-hospital and 18-month mortality. Odds ratio (OR) and 95% confidence interval (CI) were calculated. The differences were considered statistically significant at two-tailed $p < 0.05$.

RESULTS

Baseline clinical characteristics

The study included a total of 411 patients, 170 (40.9%) patients were female, 195 (40.9%) patients presented with ST-elevation. The median age was 65.0 years. The group of patients with elevated ALT and (or) AST levels differed significantly from the general sample and the controls by the incidence of ST-elevation, Killip class II–IV heart failure, higher creatinine levels, chest pain intensity, lower diastolic blood pressure, and higher troponin levels. Other that that, no significant differences between the groups were noted.

Table 1

Baseline characteristics of MI patients

Parameter	Patients, *n* = 416	Normal AST and ALT values, *n* = 297	Elevated AST and ALT, *n* = 119	*p*
Age, years, *Me* (Q_1; Q_3)	65 (56; 74)	65 (55; 74)	65 (57; 76)	0.595
Women, *n* (%)	170 (40.9)	126 (42.4)	44 (37)	0.322
ST-elevation, *n* (%)	195 (46.9)	126 (42.4)	69 (58)	0.005
History of cardiovascular diseases				
Arterial hypertension, *n* (%)	370 (88.9)	259 (87.2)	111 (93.3)	0.084
CAD, *n* (%)	177 (42.5)	132 (44.4)	45 (37.8)	0.229
Previous MI, *n* (%)	85 (20.4)	67 (22.6)	18 (15.1)	0.106
Previous myocardial revascularization, *n* (%)	49 (11.8)	40 (13.5)	9 (7.6)	0.096
Previous HF, *n* (%)	33 (7.9)	20 (6.7)	13 (10.9)	0.163
Diabetes mellitus, *n* (%)	85 (20.4)	57 (19.2)	28 (23.5)	0.347
Previous stroke, *n* (%)	32 (7.7)	20 (6.7)	12 (10.1)	0.308
Previous atrial fibrillation, *n* (%)	43 (10.3)	30 (10.1)	13 (10.9)	0.859
CKD, *n* (%)	32 (7.7)	24 (8.1)	8 (6.7)	0.839
PVD, *n* (%)	12 (2.9)	7 (2.4)	5 (4.2)	0.336

Table 1 (continued)

Parameter	Patients, *n* = 416	Normal AST and ALT values, *n* = 297	Elevated AST and ALT, *n* = 119	*p*
Chronic lung disease, *n* (%)	60 (14.4)	40 (13.5)	20 (16.8)	0.440
Peptic and duodenal ulcer, *n* (%)	39 (9.4)	30 (10.1)	9 (7.6)	0.464
Anemia, *n* (%)	107 (25.7)	72 (24.2)	35 (29.4)	0.321
Chest pain, *n* (%)	380 (91.3)	277 (93.3)	103 (86.6)	0.034
Dyspnea, *n* (%)	81 (19.5)	56 (18.9)	25 (21)	0.681
Killip class II–IV, *n* (%)	98 (23.6)	61 (20.5)	37 (31.1)	0.029
Systolic BP, mm Hg., *Me* (Q_1; Q_3)	138 (120; 160)	140 (120; 160)	130.5 (111.5; 160)	0.063
Diastolic BP, mm Hg., *Me* (Q_1; Q_3)	80 (74; 90)	80 (77; 90)	80 (67.7; 83.2)	0.005
Troponin I, ng / ml, *Me* (Q_1; Q_3)	0.39 (0.10; 2.88)	0.25 (0.09; 1.69)	1.83 (0.30; 7.45)	<0.001
Hemoglobin, g / l, *Me* (Q_1; Q_3)	137 (123; 146)	136 (123; 146)	138 (122; 148)	0.734
ALT, U / l, *Me* (Q_1; Q_3)	25 (18; 40)	21 (15; 28)	53.3 (36; 87)	<0.001
AST, U / l, *Me* (Q_1; Q_3)	29 (23; 49.2)	25 (21; 31)	77 (55; 129.9)	<0.001
Creatinine, μmol / l, *Me* (Q_1; Q_3)	95 (82; 109)	94 (81.2; 108)	96 (84; 121)	0.029
GFR < 60 ml / min / 1.73 m^2, *n* (%)	160 (39.5)	110 (37.2)	54 (45.4)	0.149
LVEF, %, *Me* (Q_1; Q_3)	45 (40; 55)	45 (40; 55)	44 (40; 53)	0.288
No lesion (stenosis) < 50% CA, *n* (%)	55 (13.2)	38 (12.8)	17 (14.3)	0.749
Three-vessel CAD, *n* (%)	203 (48.8)	153 (51.5)	50 (42)	0.084
PCI, *n* (%)	328 (78.8)	235 (79.1)	93 (78.2)	0.894
GRACE score, *Me* (Q_1; Q_3)	117 (97.2; 142.7)	116 (95.5; 140.5)	119 (99; 152)	0.081
Mortality				
In-hospital, *n* (%)	24 (5.8)	11 (3.7)	13 (10.9)	0.009
18-month, *n* (%)	47 (11.3)	27 (9.1)	20 (16.8)	0.038

Note. BP – blood pressure; PVD – peripheral vascular disease; CAD – coronary artery disease; CCI – Charlson comorbidity index; MI – myocardial infarction; CA – coronary artery; HF – heart failure; LVEF – left ventricular ejection fraction; CKD – chronic kidney disease; PCI – percutaneous coronary intervention.

Assessing the results of transaminase tests

The increase in LT levels was detected in 119 (28.6%) patients (ALT alone or AST alone in 17.8 and 25% of cases, respectively). Most of transaminase alterations were mild elevations (Table 2). In the ST-elevation subgroup, 35.4% (*n* = 69) of patients had elevated AST and ALT, 30.8% (*n* = 60) of patients had elevated AST, and 19% (*n* = 37) of the study population had elevated ALT. In non-ST-elevation subgroup, 22.6% (*n* = 50) of patients had elevated AST and ALT, 18.6% (*n* = 41) of patients had elevated AST, and 14% (*n* = 31) of the study population had elevated ALT.

Table 2

Transaminase levels in patients upon admission

Parameter	ALT, *n* = 416	AST, *n* = 416
Normal range, *n* (%)	342 (82.2)	312 (75)
1–2 times higher than ULN, *n* (%)	54 (13)	64 (15.4)
≥2–5 times higher than ULN, *n* (%)	17 (4.1)	28 (6.7)
≥5 times higher than ULN, *n* (%)	3 (0.7)	12 (2.9)

Factors associated with abnormal transaminases at baseline

The univariate analysis showed that abnormal ALT and (or) AST levels at baseline were associated with higher prevalence of ST-elevation, a higher Killip class, higher creatinine levels, and higher systolic and diastolic blood pressure.

Table 3

Univariate logistic regression analysis to assess predictors of abnormal ALT and (or) abnormal AST in patients with acute myocardial infarction

Parameter	OR	95% CI	*p*
ST-elevation (yes / no)	1.873	1.218–2.881	0.004
Systolic BP (per mm Hg)	0.993	0.986–1.0	0.04
Diastolic BP (per mm Hg)	0.979	0.964–0.994	0.007
Killip class (per class)	1.510	1.142–1.999	0.004
Creatinine (per *μmol* / l)	1.010	1.003–1.016	0.004

Abnormal liver function and outcome

All-cause mortality rates were 5.8 and 11.3% for in-hospital and 18-month mortality, respectively. Elevated ALT and AST levels were three times more common in the group of in-hospital mortality compared to patients with normal LT levels (10.9 vs. 3.7%; *p* = 0.009) and two times more common in the 18-month mortality group (16.8 vs. 9.1%, *p* = 0.038) (Table 1). Table 4 and Table 5 present

the results of the multivariate logistic regression analysis, indicating that abnormal LT levels were a significant and independent predictor of in-hospital (OR 3.607; 95% CI: 1.199–10.848; $p = 0.022$) and long-term mortality (OR 2.182; 95% CI: 1.011-4.708; $p = 0.047$). Additionally, factors associated with increased OR for in-hospital and long-term mortality included the presence of anemia, three-vessel coronary artery disease (CAD), and Killip class ≥ II. It is worth noting that older age was independently associated only with the long-term outcome.

Table 4

Multivariate logistic regression analysis of predictors of in-hospital mortality in acute myocardial infarction

Parameter	Univariate regression model OR (95% CI)	*p*	Multivariate regression model OR (95% CI)	*p*
Age (per year)	1.098 (1.051–1.147)	<0.001	1.030 (0.975–1.088)	0.287
Diabetes mellitus (yes / no)	2.495 (1.052–5.916)	0.038	1.084 (0.349–3.368)	0.889
Atrial fibrillation (yes / no)	3.198 (1.195–8.556)	0.021	2.217 (0.659–7.460)	0.198
Anemia (yes / no)	8.149 (3.277–20.268)	<0.001	3.977 (1.313–12.051)	0.015
GFR < 60 ml / min / 1.73 m² (yes / no)	4.722 (1.821–12.246)	0.001	1.439 (1.443–4.677)	0.545
Three-vessel CAD (yes / no)	4.296 (1.573–11.734)	0.004	4.572 (1.346–15.530)	0.015
Killip class ≥II (yes / no)	45.737 (10.526–198.727)	<0.001	26.432 (5.621–124.287)	<0.001
Elevated ALT and (or) AST (yes / no)	3.189 (1.386–7.337)	0.006	3.607 (1.199–10.848)	0.022

Note. GFR – glomerular filtration rate.

Table 5

Multivariate logistic regression analysis of predictors of long-term mortality in acute myocardial infarction

Parameter	Univariate regression model OR (95% CI)	*p*	Multivariate regression model OR (95% CI)	*p*
Age (per year)	1.102 (1.066–1.139)	<0.001	1.060 (1.018–1.104)	0.005
Diabetes mellitus (yes / no)	2.002 (1.028–3.898)	0.041	1.103 (0.488–2.493)	0.814
Atrial fibrillation (yes / no)	2.334 (1.041–5.234)	0.040	1.170 (0.434–3.158)	0.756
Anemia (yes / no)	5.410 (2.871–10.192)	<0.001	2.722 (1.291–5.739)	0.009
GFR < 60 ml / min / 1.73 m² (yes / no)	2.781 (1.488–5.196)	0.001	1.233 (0.549–2.739)	0.611
Three-vessel CAD (yes / no)	3.959 (1.955–8.017)	<0.001	3.260 (1.431–7.426)	0.005
Killip class ≥II (yes / no)	6.295 (3.326–11.915)	<0.001	3.397 (1.634–7.062)	0.001
Sex (female)	2.605 (1.395–4.865)	0.003	1.353 (0.592–3.091)	0.474
Previous stroke (yes / no)	4.263 (1.876–9.686)	0.001	2.333 (0.802–6.218)	0.124
Previous MI (yes / no)	2.002 (1.028–3.898)	0.041	1.237 (0.540–2.837)	0.615
Elevated ALT and (or) AST (yes / no)	2.020 (1.084–3.764)	0.027	2.182 (1.011–4.708)	0.047

DISCUSSION

The results of this study demonstrate that elevated LT levels were observed in approximately one-third of patients with AMI. Furthermore, the presence of ST-elevation, higher Killip class, lower systolic and diastolic BP, and elevated creatinine levels exhibited associations with abnormal LT levels. In addition, abnormal serum LT levels were independently associated with a worse clinical prognosis – increased risks of both in-hospital and long-term all-cause mortality.

The prevalence of elevated LT levels among AMI patients is known to vary depending on the defined cut-off values and the studied population sample. For instance, using cutoff values recommended by local guidelines (ALT > 50 U / l for men and ALT > 40 U / l for women; AST > 40 U / l for men and AST > 35 U / l for women), M. Gao et al. found elevated ALT in 38.9% and elevated AST in 71.9% of 2,417 consecutive ST-elevation MI (STEMI) patients [14]. These values are higher than the ones in our study: 19% for ALT and 30.8% for AST.

Similarly, J. Moon et al. reported the hypoxic liver injury prevalence of 22% among 456 STEMI patients undergoing primary PCI [15]. Another study reported the prevalence of increased LT of 19.5% among 1,176 STEMI patients [16]. Both studies used serum LT levels twice higher than ULN as cut-off values (> 80 U / l for ALT and > 80 U / l for AST). Using hypoxic liver injury criteria, which define hepatic injury as a sudden, transient ten-fold or

greater rise in ULN values in two or more consecutive samples for lactate dehydrogenase, ALT, and AST within 48 hours from the acute coronary event, R. Birrer et al. revealed the prevalence of hepatic injury of 27% among 87 AMI patients admitted to intensive care units [17]. Such variations underscore the importance of standardized diagnostic criteria and the need to consider patient population heterogeneity in assessing elevated LT levels in AMI.

In our study, we found that elevated LT levels were associated with signs of hypoperfusion, such as hypotension, and signs of kidney dysfunction and heart failure, including Killip Classification. This observation is in line with with previous findings [11, 14], which suggest that hepatic cell damage is linked to reduced perfusion in the centrilobular region of the liver, where blood flow is less robust due to its more distant location from the hepatic artery and portal veins. This reduction in blood flow may stem from the rapid deterioration of cardiovascular function, leading to liver ischemia.

Furthermore, the interaction between liver and heart pathophysiology shares common mechanisms with cardiorenal syndromes, such as increased venous congestion and (or) reduced cardiac output, which can exacerbate kidney function impairment [18], as demonstrated by the independent association between increased creatinine levels and elevated LTs in our study . The results of our study further support the association between elevated LT levels and unfavorable short- and long-term prognoses.

Recent studies have shown that the presence of ST-elevation is associated with elevated serum LT levels. They have also demonstrated an association between elevated serum LT levels and adverse clinical outcomes in patients with AMI [14–16, 19–21]. J. Li et al. analyzed 712 AMI patients without known liver disease, revealing the in-hospital mortality rate of 27% (n = 192). The multivariate logistic regression analysis identified that ALT ≥ 2 times higher than the ULN was an independent predictor of in-hospital mortality (OR 2.240, 95% CI 1.331–3.771; p = 0.002), while the AST level did not exhibit such an association [19].

Similar findings were reported by A. Huseynov et al., assessing the prognostic value of elevated LTs in predicting in-hospital major adverse cardiac events (MACE), defined as a composite endpoint in AMI: a need for repeated target vessel revascularization by PCI,coronary artery bypass grafting among STEMI patients, and all-cause mortality [20]. The study revealed the total in-hospital MACE rate of 9.8%, primarily driven by all-cause mortality (8.4%). In the logistic regression model, both ALT (OR 1.0018, 95% CI: 1.0008–1.0028, p = 0.0003) and AST (OR 1.0011, 95% CI: 1.0005–1.0018, p = 0.0006) were independently associated with MACE after adjusting for age and cardiac enzymes (troponin I and creatine kinase) [20].

Additionally, M. Gao et al. investigated the association of serum transaminases with 2-year mortality in 2,417 STEMI patients and found that both ALT and AST levels ≥ 95th-percentile value were associated with an increased risk of adverse outcomes (OR 1.051, 95% CI: 0.302–3.652) and (1.796, 95% CI: 0.588–5.481), respectively, after adjusting for confounding factors [14].

Several potential mechanisms were proposed to clarify the link between the elevated LT levels and the increased risk of in-hospital and long-term all-cause mortality in patients with AMI. The liver, known for its high metabolic activity and perfusion rates, is directly affected by acute circulatory changes, such as hypotension resulting from AMI, which can lead to increased levels of ALT and AST [11].

Besides, elevated LTs may occur due to hepatic congestion resulting from acute right ventricular dysfunction [22]. Current research underscores the role of factors, such as venous congestion, reduced oxygen uptake by hepatocytes, and reperfusion injury, in contributing to this LT elevation [22, 23]. While elevated serum LTs may originate from ischemic myocardial tissue, their increase often indicates secondary hypoxic liver injury, particularly common during AMI.

Furthermore, a recent meta-analysis including data from over 9.24 million participants and 242,953 cases of all-cause mortality revealed a moderately significant correlation of AST with all-cause mortality, along with geographical variations in the correlation between ALT elevation and a risk of all-cause mortality in the general population [24]. Interestingly, additional studies have documented elevation of common markers, including ALT and AST, in patients with heart failure and cardiovascular disease, wherein liver injury resulted from ischemia or congestion [25–28]. These findings further corroborate the observed association between liver

LT elevation and increased in-hospital and long-term mortality in AMI patients.

In addition to the increased LT activity, our study identified several clinical parameters associated with increased in-hospital and 18-month mortality rates in patients with AMI, which is in line with findings of earlier research [29–35]. It is worth noting that the presence of anemia, three-vessel CAD, and higher Killip class upon admission were all found to be significantly associated with adverse outcomes.

Anemia has long been recognized as a prognostic factor of poor outcomes in patients with cardiovascular diseases, including AMI. Its association with increased mortality rates is attributed to its role in exacerbating myocardial ischemia through decreased oxygen delivery to the myocardium and increased myocardial workload [31, 36, 37]. Similarly, the severity of CAD, particularly when characterized by three-vessel lesion, has consistently been linked to higher mortality rates in patients with AMI. This association is largely determined by extensive myocardial damage and an increased risk of adverse cardiac events associated with severe CA involvement [33, 38].

A higher Killip class at presentation, which reflects the severity of heart failure, has been identified as a significant predictor of mortality in AMI patients in our study. The higher Killip class was indicative of more extensive myocardial damage and hemodynamic compromise, leading to poorer outcomes [32, 39]. Additionally, age served as one of the most important risk factors for adverse outcomes in hospitalized patients with acute coronary syndrome, including AMI. Advanced age was associated with age-related physiological changes, comorbidities, and diminished physiological reserve, all of which contributed to an increased mortality risk [40]. Taken together, these findings underscore the multifactorial nature of mortality risk in patients with AMI and highlight the importance of comprehensive risk assessment incorporating clinical and demographic factors in guiding treatment strategies and improving patient outcomes.

This study had several potential limitations. Firstly, it was constrained by its single-center setting and a relatively small sample size. Secondly, despite efforts to exclude patients with various liver diseases based on medical records and risk factors potentially influencing LT levels, we admit that undiagnosed liver conditions or medications affecting liver function may have gone undetected. Additionally, the presence of AST in organs other than the liver complicates the interpretation of elevated serum LT levels, and the exact source of elevated enzymes cannot be discerned. Furthermore, liver enzyme levels were assessed only once, upon admission to the intensive care unit following revascularization, which presents another limitation.

CONCLUSION

Elevated LT levels upon admission were found in about one-third of patients presenting with AMI, which is significantly associated with ST-elevation, systolic and diastolic blood pressure, Killip class of HF, and creatinine levels. Our study showed that high LT levels were associated with an in-hospital and long-term mortality. These findings may be used for elaborating future personalized treatment strategies for AMI patients.

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