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Serum Enzymes in Myocardial Infarction Patients: A Study of Survival Time After Recovering

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Abstract

This study investigates the long-term prognostic role of serum enzyme levels in survivors of myocardial infarction (MI). We evaluated a cohort of 1496 individuals (1064 males and 432 females) aged 35-69 years, following them for a period of 14-22 years. The study aimed to elucidate the association between serum concentrations of lactate dehydrogenase (LDH), alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), and gamma-glutamyl transferase (GGT) and mortality outcomes, including all-cause mortality, cardiovascular disease (CVD), and coronary heart disease (CHD). Results revealed a statistically significant inverse association between LDH levels and mortality from all causes, CVD, and CHD. Conversely, ALT exhibited positive correlations with both CVD and all-cause mortality, and AST showed a positive association with all-cause mortality. Notably, GGT and ALP did not demonstrate any significant associations with any of the investigated mortality endpoints. Importantly, these observed relationships between serum enzyme levels and mortality outcomes remained statistically independent after adjusting for potential confounding variables such as age, sex, blood pressure, serum glucose and cholesterol levels, body mass index (BMI), smoking status, and alcohol consumption.

Keywords: Serum enzymes, Mortality, Myocardial infarction, Coronary Heart disease, Cardiovascular disease, Lactate dehydrogenase, Alanine aminotransferase, Aspartate aminotransferase

Introduction

Several serum enzymes, including alkaline phosphatase (ALP), lactate dehydrogenase (LDH), alanine aminotransferase (ALT), aspartate aminotransferase (AST), and gamma-glutamine transferase (GGT), are established markers for assessing liver dysfunction [1, 2]. However, their utility as predictors of all-cause and specific-cause mortality in the general population remains contentious, with studies yielding contrasting results [3-9].

In contrast, their role in predicting mortality among individuals with cardiovascular disease is less defined. Building upon a previous collaboration investigating the association between periodontal disease and recurrent cardiovascular events in myocardial infarction (MI) patients [10], this study delves into the relationship between the aforementioned enzymes and mortality (coronary heart disease (CHD), cardiovascular disease (CVD), and all-cause mortality) in MI survivors within the Western New York Health Study (WNYHS) cohort. Our analysis encompasses 1064 men

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and 432 women residing in New York, USA. We further assess the potential confounding effects of age, sex, alcohol consumption, smoking, and diabetes. Additionally, we examine the interactive role of LDH, ALT, and AST within individual patients to elucidate their combined impact on predicting CHD, CVD, and all-cause mortality.

Materials and Methods

Between 1996 and 2004, the Western New York Acute MI study enrolled consecutive incident myocardial infarction (MI) cases aged 35-69 years, discharged alive from hospitals in Erie and Niagara Counties, New York. Cases were defined according to World Health Organization criteria [11], excluding individuals with prior CVD. Twelve of 15 area hospitals participated, with non-participants representing primarily smaller or rural facilities where patients typically transfer to larger participants upon stabilization. To mitigate potential selection bias, we compared case ascertainment with New York State Health Department discharge data for ICD-9 codes 410.0-410.9 in the target counties, confirming our capture of approximately 95% of incident cases. Of 1496 eligible, 59.2% (n=885) consented to participate.

Incident MI determination relied on medical records and physician confirmation, adhering to World Health Organization criteria. Hospital discharge diagnoses with ICD-9 code 410 were also considered MIs [12]. Deaths and their underlying causes were ascertained from National Death Index (NDI) Plus searches through December 31, 2018.

Four months post-MI discharge, participants underwent a standardized health examination under conditions unlikely to affect the investigated serum enzymes. Anthropometric measurements included weight (beam balance scale, light clothing, no shoes) and height (tape measure), with BMI calculated as weight (kg)/height (m^2). Additionally, a computer-assisted interview assessed demographics, lifestyle, and health-related factors, including smoking and alcohol consumption. Blood samples for routine chemistry analyses were obtained between 7:30 and 9:30 AM after an 8-12 hour fast. Immediately after phlebotomy, tubes were wrapped in aluminum foil for light protection and kept at room temperature for 30 minutes to allow clotting. Blood tubes were then centrifuged at 3000 g for 10 minutes, and 1.5 mL of serum was transferred to polypropylene vials and placed in a cooler with a cold pack. Samples were delivered by courier on the same day to Millard Fillmore Center for Laboratory Medicine (Amherst, NY) for analysis. Serum enzymes LDH, ALT, AST, ALP, and GGT were measured by kinetic enzyme assays on a Paramax Automated Chemistry System [13, 14].

All methods were carried out in accordance with relevant guidelines and regulations. The study design and all the protocols were approved by the Institutional Review Board of the State University of New York in Buffalo, NY USA. The potential participants were all informed about the study design and scope, and informed consent was obtained from all subjects and/or their legal guardian(s).

Statistical Analysis

Vital status up to December 31, 2018, was ascertained through the National Death Index (NDI). Survival time was defined as the number of months between MI diagnosis and death, or censoring on December 31, 2018, for participants alive at follow-up completion. All-cause mortality encompassed any death. Specific causes of death were categorized based on ICD codes: coronary heart disease (CHD) as fatal CHD codes 410-414, 427, I20-I25, I46, I47 (underlying cause NDI), and cardiovascular disease (CVD) as fatal CVD codes 390-450, I00-I78 (underlying cause NDI). Baseline characteristics of participants were compared across LDH quartile groups using chi-square tests for categorical variables and analysis of variance (ANOVA) for continuous variables. Survival curves were generated using the Kaplan-Meier method and compared using the log-rank test. Hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated using Cox proportional hazards regression models adjusted for age, sex, body mass index (BMI), smoking status, alcohol consumption, diabetes, hypertension, dyslipidemia, hepatitis, and liver cirrhosis. All liver enzyme levels were categorized into quartiles for analyses. Statistical analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC). All tests were two-sided, with p-values < 0.05 considered statistically significant.

Results

General characteristics of patients studied

Our analysis encompassed 1496 patients who were enrolled and monitored over a 22-year period (1996-2018). While this represents the full cohort size, it's important to acknowledge potential limitations in the available data for some general patient characteristics. This is due to instances where individuals missed specific survey questions, resulting in incomplete reports. The affected characteristics are detailed in Table 1 below.

Implication of LDH, ALT, and AST on survival of MI patient groups who died from CHD, CVD, and total mortality.

This study investigated the relationship between serum enzyme levels and survival outcomes in myocardial infarction (MI) patients who succumbed to various causes, including coronary heart disease (CHD), cardiovascular disease (CVD), and overall mortality. Kaplan-Meier analysis, a robust method for survival data, was employed to identify statistically significant associations.

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Table 1: General characteristics of our studied patients

Total number of patients studied: 1496*		
Characteristics	**n**	**%**
Age (n=1496)		
35-39	61	4.08
40-64	1196	79.95
65 and over	239	15.97
Gender (n=1496)		
Female	432	28.88
Male	1064	71.12
Smoking status (n=1485)		
Never smoker	373	25.11
Former smoker	849	57.18
Current smoker	263	17.71
Drinking status (n=1491)		
Abstainers	113	7.58
Non-Current Drinkers	522	35.01
Current Non-Weekly Drinkers	313	20.99
Current Weekly Drinkers	543	36.42
Have/had diabetes (n=1479)		
No	1229	83.1
Yes	250	16.9
Have/had high blood pressure (n=1477)		
No	717	48.54
Yes	760	51.46
Have/had high blood cholesterol (n=1455)		
No	456	31.34
Yes	99	68.66

*Except for age and gender, survey questions about other characteristis were not fully answered, so the number of patients for each factor is different.

CHD mortality:

- Only lactate dehydrogenase (LDH) levels exhibited a statistically significant correlation with CHD mortality.
- Increased LDH levels were associated with a reduced survival time, suggesting its potential as a predictor of CHD mortality in MI patients.

CVD mortality:

- LDH and alanine aminotransferase (ALT) levels emerged as statistically significant factors influencing CVD mortality.
- Similar to CHD, elevated LDH levels shortened survival, while higher ALT levels paradoxically coincided with an improved survival prognosis. Further investigation is warranted to elucidate the underlying mechanisms driving this unexpected association.

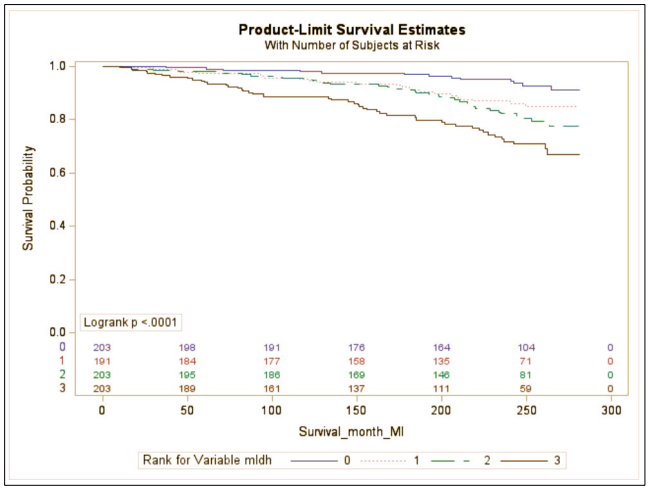

Figure 1: Kaplan-Meier survival curves for CHD mortality according to quartiles of LDH

Total mortality:

- LDH, ALT, and aspartate aminotransferase (AST) levels all demonstrated statistically significant correlations with overall mortality.
- Consistent with the findings for CHD, increased LDH levels portended a poorer prognosis,whereas higher ALT and AST levels were associated with extended survival. These observations align with the results seen in CVD mortality analysis and necessitate further research to unravel the biological explanations.

In general, this study highlights the crucial role of LDH as a predictor of survival across CHD, CVD, and overall mortality in MI patients. Higher LDH levels consistently translate to a shorter lifespan. Conversely, the positive associations observed between ALT and AST levels and survival outcomes, particularly in CVD and total mortality analyses, warrant further exploration. Unraveling the mechanisms behind these intriguing findings holds the potential to refine prognostic models and personalize treatment strategies for improved patient outcomes in the context of MI.

Basic characteristics of study subjects observed with LDH enzyme level quartiles.

Given the pivotal role of LDH as highlighted by the preceding findings, we further investigated the baseline characteristics of the study subjects stratified by quartiles of serum lactate dehydrogenase (LDH) levels. The results for the teacher cohort are presented in Table 2.

Consistent with the trends observed, higher quartiles of serum lactate dehydrogenase (LDH) levels are associated with a greater proportion of female participants and higher body mass indices (BMIs) compared to lower quartiles. Interestingly, across all quartile groups, the prevalence

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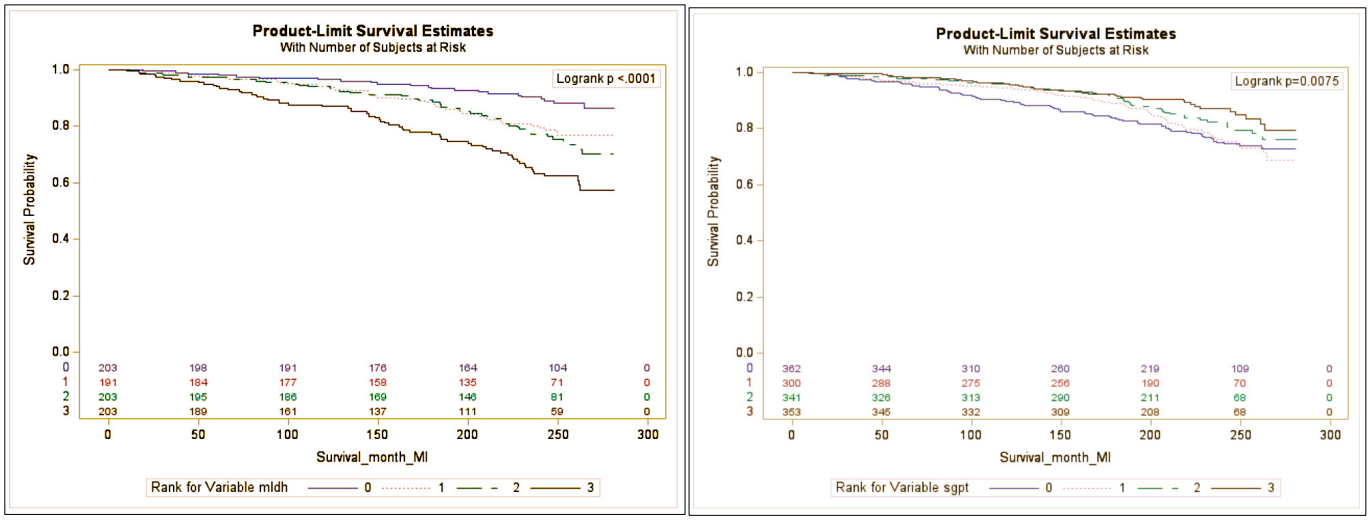
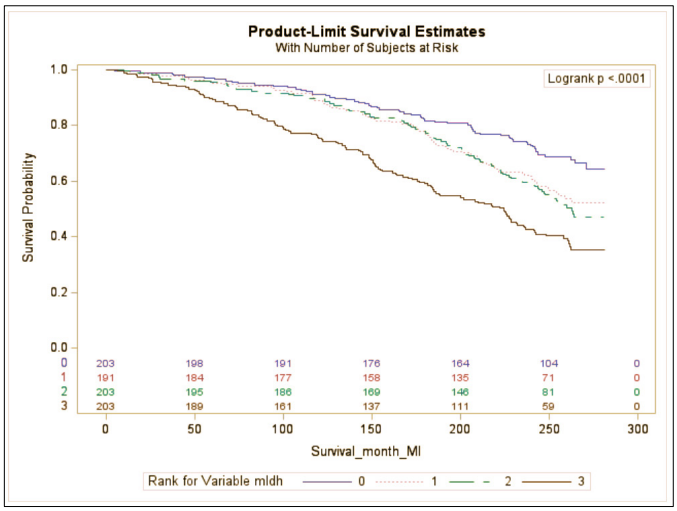
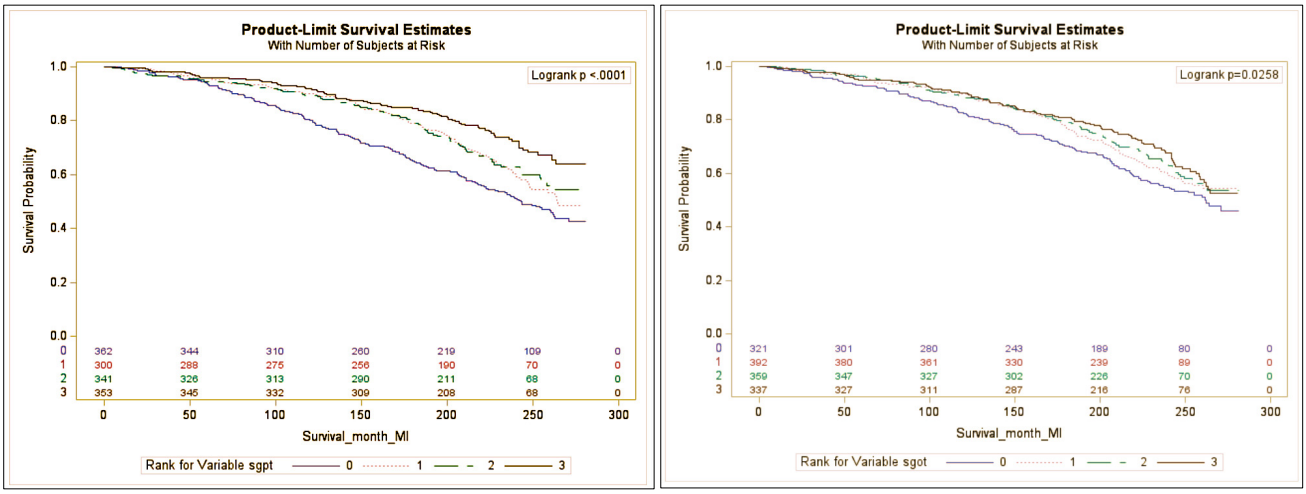


2 (A) 2(B)

Figure 2: Kaplan-Meier survival curves for CVD mortality according to quartiles of the 2 enzymes. LDH: 2(A); ALT: 2(B).



3(A)



3(B) 3(C)

Figure 3: Kaplan-Meier survival curves for total mortality according to quartiles of the 3 enzymes. LDH: 3(A); ALT: 3(B); AST: 3(C).

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of smokers significantly outweighs that of non-smokers. Additionally, a positive correlation emerges between systolic blood pressure (SBP) and cholesterol levels with LDH concentrations, such that higher LDH levels coincide with increased SBP and cholesterol values. Notably, no significant relationship is observed between LDH levels and either diastolic blood pressure (DBP) or glucose levels.

Implications of LDH, ALT, and AST in the cases of CHD, CVD, and total mortality

Through robust statistical methods, we have established a statistically significant association between the concentrations of LDH, ALT, and AST enzymes and time to event, as evidenced by the detailed results presented in Table 3.

Table 3 demonstrates a clear association between all three enzymes and patient survival time. While lactate dehydrogenase (LDH) exhibited a negative correlation, meaning higher enzyme levels were associated with reduced survival time, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) displayed positive correlations, indicating longer survival times with higher enzyme levels. To further elucidate these correlations, hazard ratios (HRs) are presented in Table 4.

Table 4 presents the multivariable hazard ratios (HRs) derived from Cox proportional hazards regression analyses. These models adjusted for potential confounders such as age, sex, body mass index (BMI), smoking history, alcohol consumption, diabetes, hypertension, dyslipidemia, hepatitis, and liver cirrhosis. Notably, LDH exhibited a statistically significant independent and direct association with time to death across all-cause, cardiovascular disease (CVD), and coronary heart disease (CHD) mortality. Participants in the highest quartile of the LDH distribution displayed HRs of 5.50, 4.80, and 2.62 for CHD, CVD, and all-cause mortality, respectively. While AST and ALT also displayed trends of inverse associations with mortality, none of the estimated HRs reached statistical significance. Furthermore, the De Ritis ratio (AST/ALT) did not offer any significant improvement in the model performance.

Follow up time and influence of vital status factors

During our study period, 575 of the 1496 study participants died. Total follow-up time ranged from 4.7 to 281.4 months, with a mean survival time of 201.2 months (standard deviation: 62.2).

Table 2: Baseline characteristics of study subjects according to the qurtiles of lactate dehydrogenate (LDH)

	Q1	Q2	Q3	Q4	p
	n = 204	n = 192	n = 204	n = 204	
Serum level (Mean ± SD U/L)	112.2 ± 11.8	130.9 ± 4.5	147.3 ± 5.0	181.8 ± 25.6	<.0001
Age (y)	53.8 ± 8.7	54.9 ± 8.7	55.2 ± 9	55.9 ± 9.1	0.254
Gender					0.013
Female (n/%)	44 /21.6	45/23.4	62/30.4	70/34.3	
Male (n/%)	160/78.4	147/76.6	142/69.6	134/65.7	
BMI* (kg/m2)	28.3 ± 4.4	28.7 ± 4.6	29.6 ± 5.6	29.4 ± 4.9	0.0218
SBP* (mmHg)	112.7 ± 13.6	115.9 ± 15.4	115.3 ± 15.8	117.0 ± 17.1	0.0388
DBP* (mmHg)	70.1 ± 8.5	70.6 ± 9.2	71.1 ± 9.3	71.0 ± 9.8	0.6621
Glucose (mg/dL)	108.7 ± 34.9	110.8 ± 36.7	115.3 ± 41.1	115.4 ± 47.6	0.247
Cholesterol (mg/dL)	190.7 ± 35.1	197.5 ± 41.8	203.4 ± 46.2	203.8 ± 42.2	0.0042
Smoking state					0.019
Never smokers (n/%)	46/22.9	42/21.9	39/19.1	46/22.7	
Former smokers (n/%)	112/55.7	102/53.1	128/62.7	134/66.0	
Current smokers (n/%)	43/21.4	48/25.0	37/18.1	23/11.3	
Drinking state					0.855
Abstainers and irregular abstainers (n/%)	11/5.4	09/4.7	14/6.8	17/8.4	
Non-current drinkers (n/%)	68/33.7	68/35.4	71/35.0	82/40.2	
Current drinkers (n/%)	123/60.9	115/59.9	118/58.2	105/51.4	

*BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure

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To assess the potential influence of investigated vital status factors on survival outcomes, we constructed a table contrasting these factors with the binary endpoint of alive or deceased at the study point (Table 5).

Table 5 details the post-myocardial infarction (MI) mortality rates stratified by baseline characteristics and medical conditions. Interestingly, compared to ongoing smokers, patients who had quit smoking displayed a significantly lower mortality rate. Notably, the lowest mortality rate was observed among non-smokers. Similarly, the presence of diabetes and hypertension were independently associated with elevated mortality after MI.

Influence of Post-MI Medications on Liver Enzymes and Survival

While the impact of antibiotics, aspirin, and lipid-lowering drugs on liver enzymes in post-myocardial infarction (MI) patients is intricate and multifaceted, their potential role in influencing ALT and AST levels warrants closer examination. Our data revealed no significant differences in the proportions of patients across ALT and AST quartiles utilizing these medications (Table 6 and Table 7). This suggests that their effect on these enzymes, and consequently on survival time within each quartile group, might be minimal or not readily detectable through our analysis.

Table 3: Serum levels of LDH, ALT và AST (Mean ± SD) and duration to events according to their quartiles

	Q1	Q2	Q3	Q4	Normal range
LDH levels (U/L)	112.2 ± 11.8	130.9 ± 4.5	147.3 ± 5.0	181.8 ± 25.6	100-190 U/L
Time to event according to LDH levels (months)	228.5 ± 60.2	215.6 ± 64.3	215.8 ± 65.9	185.5 ± 60.3	
ALT levels (U/L)	11.6 ± 2.8	18.1 ± 1.4	24.0 ± 2.2	42.3 ± 25.5	7-56 U/L
Time to event according to ALT levels (months)	195.5 ± 73.7	205.2 ± 58.8	200.5 ± 60.0	202.9 ± 53.9	
AST levels (U/L)	16.7 ± 2.2	21.5 ± 1.1	25.6 ± 1.4	36.8 ± 15.2	0-50 U/L
Time to event according to AST levels (months)	195.4 ± 70.5	202.2 ± 60.0	202.2 ± 58.0	204.1 ± 58.9	

Table 4: Hazard ratios and 95% confidence intervals for time to event according to quartiles of enzymes*.

Effect of LDH, ALT, and AST on mortality						
	CHD Mortality		CVD Mortality		Total Mortality	
	Event (n)	HR (95% CI)	Event (n)	HR (95% CI)	Event (n)	HR (95% CI)
LDH						
Quartile 1	13	1	19	1	62	1
Quartile 2	23	2.08 (1.04-4.13)	37	2.29 (1.31-4.00)	82	1.49 (1.06-2.07)
Quartile 3	33	2.95 (1.55-5.64)	42	2.51 (1.45-4.33)	91	1.61 (1.16-2.23)
Quartile 4	45	5.50 (2.92-10.33)	60	4.80 (2.83-8.15)	119	2.62 (1.91-3.61)
ALT						
Quartile 1	52	1	70	1	175	1
Quartile 2	35	0.80 (0.52-1.24)	59	1.01 (0.71-1.44)	114	0.81 (0.64-1.03)
Quartile 3	38	0.94 (0.61-1.45)	50	0.91 (0.62-1.32)	119	0.91 (0.71-1.16)
Quartile 4	30	0.70 (0.43-1.12)	38	0.66 (0.44-1.002)	85	0.66 (0.50-0.86)
AST						
Quartile 1	41	1	58	1	133	1
Quartile 2	44	0.82 (0.53-1.26)	63	0.84 (0.59-1.20)	144	0.84 (0.66-1.07)
Quartile 3	36	0.79 (0.50-1.24)	52	0.82 (0.56-1.20)	125	0.89 (0.70-1.14)
Quartile 4	38	0.94 (0.60-1.48)	49	0.86 (0.59-1.27)	107	0.85 (0.65-1.10)
AST/ALT						
Quartile 1	27	1	37	1	85	1
Quartile 2	34	1.06 (0.64-1.77)	45	1.01 (0.65-1.57)	99	0.90 (0.67-1.21)
Quartile 3	48	1.54 (0.95-2.50)	66	1.54 (1.02-2.33)	139	1.32 (0.99-1.74)
Quartile 4	46	1.39 (0.84-2.29)	69	1.49 (0.97-2.27)	169	1.39 (1.05-1.83)

*LDH/ALT/AST was grouped based on quartiles among only those with non-missing relevant enzymes, survival time and all covariates. HR: Hazard ratio was adjusted for age, sex, body mass index, smoking, alcohol, diabetes, hypertension, dyslipidemia, hepatitis, and liver cirrhosis.

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Table 5: Relationship between Investigated Factors and Patient Survival Status

	Was the participant dead?			
	N	0: no	1: yes	p-value (Chi-square Test)
		n (%)	n (%)	
Total	1496	921 (61.6%)	575 (38.4%)	
Age				<.001
1: 35-39	61	46 (75.4%)	15 (24.6%)	
2: 40-64	1196	781 (65.3%)	415 (34.7%)	
3: 65 and over	239	94 (39.3%)	145 (60.7%)	
Gender				0.001
Female	432	238 (55.1%)	194 (44.9%)	
Male	1064	683 (64.2%)	381 (35.8%)	
Smoking status				<.001
Never smoker	373	260 (69.7%)	113 (30.3%)	
Former smoker	849	536 (63.1%)	313 (36.9%)	
current smoker	263	118 (44.9%)	145 (55.1%)	
Drinking status				<.001
Abstainers	113	70 (61.9%)	43 (38.1%)	
Non-Current Drinkers	522	287 (55.0%)	235 (45.0%)	
Current Non-Weekly Drinkers	313	209 (66.8%)	104 (33.2%)	
Current Weekly Drinkers	543	353 (65.0%)	190 (35.0%)	
Have/had diabetes				<.001
No	1229	819 (74.7%)	410 (25.3%)	
Yes	250	94 (37.6%)	156 (62.4%)	
Have/had high blood pressure				<.001
No	717	488 (68.1%)	229 (31.9%)	
Yes	760	422 (55.5%)	338 (44.5%)	
Have/had high blood cholesterol				0.023
No	456	258 (56.6%)	198 (43.4%)	
Yes	999	639 (64.0%)	360 (36.0%)	

Table 6: Status of using antibiotics, aspirin, and lipid-lowering drugs in the group of patients having ALT quantification.

	Q1	Q2	Q3	Q4	*p*
Percentage of antibiotics users (n/%)	12/33.33	18/6.00	27/7.89	25/7.04	0.0895
Percentage of aspirin users (n/%)	289/80.28	261/87.00	287/83.92	283/79.72	0.0937
Percentage of lipid lowering drugs users (n/%)	172/47.77	186/62.00	229/66.96	264/74.37	0.2124

Table 7: Status of using antibiotics, aspirin, and lipid-lowering drugs in the group of patients having AST quantification.

	Q1	Q2	Q3	Q4	*p*
Percentage of antibiotics users (n/%)	15/4.70	23/5.88	25/6.92	23/6.78	0.5159
Percentage of aspirin users (n/%)	267/83.70	330/84.40	295/81.72	272/80.24	0.398
Percentage of lipid lowering drugs users (n/%)	175/54.85	249/63.69	240/66,48	225/66.37	0.0156

Discussion

Post-Myocardial Infarction Mortality: Exploring the Roles of LDH, ALT, and AST

This prospective follow-up study investigated the potential of five liver enzymes (lactate dehydrogenase (LDH), gamma-glutamyl transferase (GGT), alkaline phosphatase (ALP), alanine aminotransferase (ALT), and aspartate aminotransferase (AST) to predict all-cause, cardiovascular disease (CVD), and coronary heart disease (CHD) mortality in patients who survived and recovered from an acute myocardial infarction (MI). Initial analyses revealed no significant association between survival time and GGT or ALP levels. Therefore, we focused subsequent analyses on the remaining three enzymes: LDH, ALT, and AST.

Rationale for Focusing on LDH, ALT, and AST:

- LDH is a well-established marker of tissue damage, including myocardial injury.
- ALT and AST are primarily involved in liver function, but elevated levels can also indicate cellular injury in other organs, including the heart.
- Prior studies have suggested potential associations between LDH, ALT, and AST levels and cardiovascular outcomes.

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By focusing on these three enzymes, we aimed to gain a deeper understanding of their potential role in predicting mortality after MI and to identify potential clinical implications for patient management. Lactate dehydrogenase (LDH), a cytoplasmic enzyme, is abundant across various tissues, with particularly high concentrations in muscle, liver, and kidney. Numerous conditions can elevate serum LDH, including liver disease, anemia, myocardial infarction, bone fractures, muscle trauma, malignancies, and infections like encephalitis, meningitis, and HIV. Notably, serum LDH levels typically return to normal range during patient recovery [15]. In our cohort of recovered myocardial infarction (MI) patients, we observed a robust association between elevated serum LDH and shorter survival time across all-cause, cardiovascular disease (CVD), and coronary heart disease (CHD) mortality (Figures 1, 2, and 3). While previous studies have investigated LDH in acute MI for several years [16, 17], this relationship with long-term survival in recovered MI patients seems largely unexplored. In our study, the link between LDH and mortality might, at least partly, reflect its potential as an indirect marker of cardiac damage and infarct size [15].

In addition to LDH, our analysis revealed significant associations between serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels and survival time in MI patients. This finding aligns with previous studies demonstrating clear linkages between ALT and AST levels and mortality in the context of acute myocardial infarction (AMI) [18-20]. However, a key distinction between our study and the aforementioned research lies in the timing of enzyme measurements. While past studies measured enzyme levels during hospitalization for AMI, our investigation quantified enzymatic activity four months after patient recovery, a timeframe beyond the typical duration of elevated serological markers associated with the acute illness. Notably, no prior studies have examined liver enzyme levels in fully recovered MI patients. Furthermore, a distinct and intriguing observation in our study is the positive correlation between ALT and AST levels and various mortality endpoints. This indicates that, within the normal range or marginally elevated levels observed in our cohort (Table 2), higher ALT or AST concentrations are associated with longer survival times.

Potential Influence of Post-MI Medications on Liver Enzyme Levels and Survival

While elevated ALT and AST could potentially be attributed to post-MI therapeutic regimens, including antibiotics, aspirin, or lipid-lowering drugs, our analysis did not reveal any significant differences in the utilization of these medications across ALT and AST quartiles (Tables 5 and 6). Notably, the only statistically significant difference ($p=0.0156$) observed among quartile groups was a gradual increase in lipid-lowering drug use among patients with higher AST levels. This intriguing finding suggests that, despite a marginal elevation in AST, lipid-lowering therapy might possibly contribute to improved health outcomes and longer survival times. This aligns with recent research advocating for statin use to prevent future cardiovascular disease (CVD) morbidity and mortality based on estimated 10-year CVD risk [17, 18], and further underscores the potential clinical benefits of such therapies even in the context of slightly elevated liver enzymes.

The Influence of Individual Factors on Mortality Outcomes in Myocardial Infarction Patients

Our analysis identified gender as a significant factor influencing the association between serum lactate dehydrogenase (LDH) levels and mortality in MI patients (Table 1). This finding aligns with previous research highlighting the impact of gender on post-MI survival. Although increased age is recognized as a major risk factor, several studies suggest that it does not fully explain the higher mortality observed in women [21-24]. Interestingly, our data also shows a higher number of deaths among women compared to men (Table 4). However, further investigations with larger cohorts are warranted to reconcile these findings and provide a more nuanced understanding of gender-specific mortality following MI.

Regarding the role of serum cholesterol, our study revealed a positive correlation between total cholesterol concentrations and LDH quartiles (Table 1). However, the relevance of cholesterol as a risk factor for all-cause and cardiovascular mortality in older populations remains somewhat controversial [25-28]. Our results in Table 4 further illuminate this complexity, showing that patients with higher cholesterol levels paradoxically exhibit lower mortality rates. This potentially reflects the influence of cholesterol-lowering medications, which might have contributed to extended survival times. Smoking is a leading preventable cause of mortality, claiming over 400,000 lives annually in the United States, with a notable impact on cardiovascular deaths. Coronary artery disease patients who continue smoking face a considerably higher risk of death due to the detrimental effects of smoking on coronary blood flow, myocardial oxygen demand, and thrombosis risk [29-34]. Conversely, smoking cessation after a myocardial infarction demonstrably reduces mortality risk [35]. Consistent with these findings, our study reveals that patients who have quit smoking show lower mortality rates compared to current smokers, with non-smokers exhibiting the lowest risk (Table 4). Notably, these results reiterate the well-established risk profile associated with smoking in MI patients and highlight the importance of emphasizing smoking cessation as a critical intervention strategy. Despite numerous studies regarding the predictive role of GGT in the mortality of MI patients [4][36], our study

did not find an impact of GGT on the survival time of patients after MI.

Limitations of the Study

First, despite trying to eliminate variables affecting CHD mortality, CVD mortality, and total mortality, it was not possible to remove these and some other residual or unmeasured confounding factors. Second, we only analyzed serum enzyme levels at four months following the patient's recovery and discharge and other variables were also recorded at this point (i.e., when the patient had many different behavioral changes after treatment compared to before, such as smoking habits, alcohol consumption, and comorbidities also improved during MI treatment). In addition, over the course of time from that time until we ended the research, we could not investigate lifestyle changes that may affect the patients' survival time. Third, a possibility exists that over 8 years, serum enzymes were measured with different chemical kits or assays. This may mean that the normal range of these enzymes and assay results may slightly differ. However, it is noteworthy that the assay results of each method are known to be highly correlated. Furthermore, the laboratory has been subjected to mandatory internal and external quality control. Despite this, our study has its own strengths, namely a large enough population to be able to gather data for epidemiological assessments, as well as related data systems such as demographics and laboratory information. Tests, medical diagnoses, and medications are always available to satisfy the needs of discussion. As a result, we performed comprehensive analyses on the effects of LDH, ALT, and AST on the mortality of post-recovered MI patients.

Conclusion

1. LDH shows a strong association with all kinds of mortality and can be used as a predictor for CHD, CVD, and total mortality. ALT is also associated with CVD as well as all-cause mortality, while AST has only been shown to be associated with all-cause mortality. Our study did not find that GGT and ALP had an impact on MI survivors' outcome.
2. Age, gender, smoking, drinking, diabetes, high blood pressure, high blood cholesterol level are risk factors of mortality in general.

Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Author Contributions

HDC ideated and wrote the manuscript. DTBT, MA, and DNK contributed to manuscript writing and editing. JN, HDC, and DTBT contributed to manuscript writing and figures drawing. HDC, DTBT, JF and MT contributed to manuscript ideation, revision, and editing.

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