GMR
The Original

COMPARATIVE EVALUATION OF LP-PLA2 AND MANNOSE-BINDING LECTIN AS INFLAMMATORY AND COMPLEMENT-RELATED BIOMARKERS IN EARLY MYOCARDIAL INFARCTION: A CASE-CONTROL STUDY

Yosra Adil Abd-Al-Hussein Al-Saeedi[1], Mohammed Imran Hamzeh[1], Moayed Basheer Hamid[2]

[1] Department of Chemistry and Biochemistry, College of Medicine, Al-Nahrain University, Baghdad, Iraq
[2] Interventional Cardiology, Baghdad, Iraq

ABSTRACT
Background: Early myocardial infarction involves plaque disruption, lipid-mediated inflammation, sterile inflammatory signaling and myocardial injury. Lp-PLA2 is associated with oxidized lipoproteins and plaque inflammation, whereas mannose-binding lectin (MBL) contributes to lectin complement pathway activation. Their circulating concentrations may not fully represent local pathway activity, but they can provide useful information about early inflammatory and complement-related responses.
Objective: To compare serum Lp-PLA2 and MBL concentrations in early MI and evaluate their diagnostic performance for differentiating MI from healthy controls and STEMI from NSTEMI.
Methods: This case-control study included 132 participants: 90 patients with MI (58 STEMI and 32 NSTEMI) and 42 healthy controls. Serum Lp-PLA2 concentration and MBL concentration were measured by ELISA. Group differences were analyzed using non-parametric statistics, and diagnostic discrimination was assessed by ROC analysis.
Results: Lp-PLA2 concentration was significantly lower in both MI subgroups compared with controls (Kruskal-Wallis H = 15.65, $p < 0.001$). Median Lp-PLA2 was 10.59 ng/mL in controls, 10.06 ng/mL in NSTEMI and 9.95 ng/mL in STEMI. MBL showed no significant difference across groups (H = 1.99, p = 0.369), with medians of 69.34, 68.79 and 70.03 ug/L in controls, NSTEMI and STEMI, respectively. For total MI versus controls, Lp-PLA2 showed moderate discrimination (AUC = 0.714; 95% CI 0.611-0.809; cutoff <=10.56 ng/mL; sensitivity 80.0%; specificity 54.8%), whereas MBL was non-discriminatory (AUC = 0.516; 95% CI 0.397-0.633).
Conclusion: Serum Lp-PLA2 concentration was reduced in early MI and showed moderate diagnostic performance, while serum MBL concentration was not diagnostically useful in this cohort. The findings emphasize the need to distinguish circulating biomarker concentration from local inflammatory or complement pathway activity.

KEYWORDS: Lp-PLA2; mannose-binding lectin; complement; vascular inflammation; myocardial infarction; STEMI; NSTEMI; ROC analysis

1. INTRODUCTION

Myocardial infarction is usually caused by acute coronary plaque disruption with thrombosis or severe flow limitation. Diagnosis remains based on the clinical setting, ECG findings and cardiac troponin dynamics (Thygesen et al., 2018). At the same time, MI is not only a necrosis event; it also involves lipid oxidation, vascular inflammation, endothelial activation, complement responses and tissue repair.

Lp-PLA2 is linked to circulating lipoproteins, especially LDL, and hydrolyzes oxidized phospholipids to generate inflammatory lipid mediators. It has been studied in relation to plaque burden, plaque instability, acute coronary syndrome and future vascular risk (Lp-PLA2 Studies Collaboration et al., 2010; Chung et al., 2014). However, the direction and strength of association can vary according to whether mass or activity is measured, the timing of blood collection, and whether the study involves stable coronary disease or acute MI (Elkind et al., 2009).

MBL is a circulating pattern-recognition molecule that can initiate the lectin complement pathway. Experimental studies support a role for MBL in myocardial ischemia-reperfusion injury (Jordan et al., 2001; Walsh et al., 2005; Busche et al., 2009), and clinical work has examined MBL and complement markers in coronary artery disease (da Rosa et al., 2024). A serum concentration result, however, does not capture MBL2 genotype, functional activity, MASP activation, complement fragments or local tissue deposition.

This article presents Lp-PLA2 and MBL together because they represent two different inflammatory pathways: lipid-associated vascular inflammation and complement-related innate immunity. The intention is not to force both markers into

a diagnostic claim, but to report a balanced inflammatory/complement profile from the thesis dataset, including one significant and one negative finding.

2. MATERIALS AND METHODS

2.1 Study design and population

This case-control study was conducted in the Department of Chemistry and Biochemistry, College of Medicine, Al-Nahrain University, Baghdad, Iraq. Samples were collected from the coronary care unit and cardiology department of Ibn Al-Nafees Teaching Hospital and Al-Imamain Al-Kadhimain Medical City, Baghdad, Iraq, from September 2025 to December 2025. The study population consisted of 132 individuals aged 40-70 years, including 90 early MI patients and 42 apparently healthy controls. MI patients were classified into 58 STEMI and 32 NSTEMI patients according to clinical and electrocardiographic diagnosis.

2.2 Clinical and laboratory procedures

Clinical information included smoking status, diabetes mellitus, hypertension, dyslipidemia history and time from symptom onset to sample collection. Blood was obtained during the early diagnostic phase. Serum was separated, visually inspected, aliquoted and stored at -20°C until measurement.

2.3 Biomarker assays

Serum Lp-PLA2 concentration and MBL concentration were quantified by ELISA according to the manufacturer instructions. Lp-PLA2 was reported in ng/mL and MBL in ug/L. The Lp-PLA2 assay measured concentration rather than enzymatic activity, which is important for interpretation.

2.4 Statistical analysis

Biomarker distributions were non-normal; therefore, results are presented as median (IQR). Kruskal-Wallis testing was used for overall group comparisons, followed by pairwise non-parametric comparisons when appropriate. ROC analysis was used to assess discrimination between total MI and controls, between each MI subtype and controls, and between STEMI and NSTEMI. A p value <0.05 was considered statistically significant.

3. RESULTS

3.1 Serum Lp-PLA2 and MBL concentrations

Lp-PLA2 concentration was highest in the control group and significantly lower in both MI subgroups. MBL concentrations were similar across controls, NSTEMI and STEMI, and the overall comparison was not significant.

Table 1. Serum Lp-PLA2 and MBL concentrations by diagnostic group.

Biomarker	Control (n=42)	NSTEMI (n=32)	STEMI (n=58)	H	p
Lp-PLA2 (ng/mL)	10.59 (9.98-12.45)	10.06 (9.70-10.40)	9.95 (9.44-10.54)	15.65	<0.001
MBL (ug/L)	69.34 (63.43-75.62)	68.79 (63.70-72.78)	70.03 (66.00-75.57)	1.99	0.369

Values are median (IQR). H = Kruskal-Wallis statistic.

Pairwise analysis showed that Lp-PLA2 was significantly lower in NSTEMI compared with controls ($U = 955$, $p = 0.002$, $r = -0.421$) and in STEMI compared with controls ($U = 1744$, $p < 0.001$, $r = -0.432$). STEMI and NSTEMI did not differ significantly ($U = 950$, $p = 0.853$). For MBL, pairwise comparisons were not significant.

3.2 ROC analysis for MI versus healthy controls

For total MI versus controls, Lp-PLA2 showed moderate diagnostic performance. A lower concentration predicted MI at a cutoff of <=10.56 ng/mL. MBL had an AUC close to 0.50 and low specificity at the selected cutoff, indicating little diagnostic value in this dataset.

Table 2. ROC performance for differentiating MI patients from healthy controls.

Biomarker	AUC	95% CI	Optimal cutoff	Sensitivity	Specificity
Lp-PLA2 (ng/mL)	0.714	0.611-0.809	<=10.56	80.0%	54.8%
MBL (ug/L)	0.516	0.397-0.633	>63.07	90.0%	26.2%

AUC = area under the ROC curve. Cutoff direction indicates values predicting MI.

3.3 ROC analysis by MI subtype

Lp-PLA2 showed similar moderate performance for NSTEMI versus controls and STEMI versus controls. MBL remained non-discriminatory in both subtype-control comparisons. Neither marker reliably separated STEMI from NSTEMI, suggesting that the Lp-PLA2 signal relates to MI versus health rather than to ECG-defined subtype.

Table 3. ROC performance by MI subtype versus controls.

Comparison	Lp-PLA2 AUC	MBL AUC	Main interpretation
NSTEMI vs control	0.711	0.526	Lp-PLA2 was moderate; MBL was non-discriminatory.
STEMI vs control	0.716	0.540	Lp-PLA2 was moderate; MBL was non-discriminatory.
STEMI vs NSTEMI	0.512	0.598	Both markers showed limited separation between MI subtypes.

4. DISCUSSION

The main finding of this article is a contrasting inflammatory/complement profile in early MI. Serum Lp-PLA2 concentration was significantly lower in both STEMI and NSTEMI than in controls, while serum MBL concentration did not differ significantly among the groups. This result is useful because it separates a measurable serum signal from a biologically plausible but non-discriminatory marker.

The decreased Lp-PLA2 concentration should be interpreted carefully. Many studies of coronary artery disease and acute coronary syndrome have linked higher Lp-PLA2 mass or activity with plaque burden and instability (Lp-PLA2 Studies Collaboration et al., 2010; Chung et al., 2014). The lower concentration observed here may be related to the early sampling window, redistribution toward inflamed or ruptured plaques, binding to altered lipoprotein fractions, treatment effects, or the difference between concentration and enzymatic activity assays. Therefore, the present result should be stated as reduced serum Lp-PLA2 concentration in early MI, not as reduced Lp-PLA2 biological activity.

The ROC findings support a cautious interpretation. Lp-PLA2 achieved a moderate AUC of 0.714 for MI versus controls, with good sensitivity but limited specificity. This pattern is more suitable for a supportive research biomarker than for a stand-alone diagnostic test. The lack of separation between STEMI and NSTEMI indicates that Lp-PLA2 may reflect a shared MI-related inflammatory process rather than the electrocardiographic pattern of infarction.

MBL was not significantly different among controls, NSTEMI and STEMI, and its ROC performance was close to chance. This negative finding does not exclude involvement of the lectin complement pathway in myocardial ischemia or reperfusion injury. Serum MBL concentration is influenced by genotype and baseline immune variation and does not necessarily reflect MBL function, MASP activation, complement cleavage products or local deposition in injured tissue.

The combined interpretation is therefore straightforward: Lp-PLA2 provided a measurable serum difference in this early MI cohort, whereas MBL concentration did not. The article should avoid presenting MBL as a diagnostic marker. Its value here is as an informative negative result, suggesting that complement-related assessment may require functional assays or downstream activation markers rather than total serum MBL concentration alone.

5. Limitations

- The comparison with healthy controls may not reflect real-world chest-pain differential diagnosis.
- Lp-PLA2 was measured as serum concentration rather than enzymatic activity.
- MBL concentration does not capture MBL function, MBL2 genotype, MASP activation or complement activation products.
- The single-sample design cannot define early, peak or recovery-phase kinetics.
- Larger prospective studies with clinically relevant control groups are required to validate the Lp-PLA2 finding.

6. CONCLUSION

Serum Lp-PLA2 concentration was significantly lower in early MI and showed moderate diagnostic performance for MI versus controls. Serum MBL concentration was not significantly different among groups and had limited diagnostic value. These findings support Lp-PLA2 as an exploratory supportive marker of lipid-associated vascular inflammation and suggest that MBL should be investigated through functional complement assays or downstream activation markers rather than concentration alone.

Declarations

Ethics approval: The thesis study was approved by the Scientific and Ethical Committee of the College of Medicine, Al-Nahrain University. The exact approval number should be inserted before journal submission.

Consent to participate: Informed consent was obtained according to the approved study protocol.

Conflict of interest: The authors declare no conflict of interest. This statement should be confirmed by all authors before submission.

Funding: No specific funding is declared. This statement should be modified if funding support was received.

Data availability: The datasets are available from the corresponding author on reasonable request, subject to ethical approval and participant confidentiality.

REFERENCES

1. Thygesen, K., Alpert, J.S., Jaffe, A.S., Chaitman, B.R., Bax, J.J., Morrow, D.A. and White, H.D. (2018) 'Fourth Universal Definition of Myocardial Infarction (2018)', Circulation, 138(20), pp. e618-e651. doi:10.1161/CIR.0000000000000617.

2. Lp-PLA2 Studies Collaboration, Thompson, A., Gao, P., Orfei, L., Watson, S., Di Angelantonio, E., Kaptoge, S., Ballantyne, C., Cannon, C.P., Criqui, M., et al. (2010) 'Lipoprotein-associated phospholipase A2 and risk of coronary disease, stroke, and mortality: collaborative analysis of 32 prospective studies', The Lancet, 375(9725), pp. 1536-1544. doi:10.1016/S0140-6736(10)60319-4.

3. Chung, H., Kwon, H.M., Kim, J.Y., Yoon, Y.W., Rhee, J., Choi, E.Y., Min, P.K., Hong, B.K., Rim, S.J., Yoon, J.H., et al. (2014) 'Lipoprotein-associated phospholipase A2 is related to plaque stability and is a potential biomarker for acute coronary syndrome', Yonsei Medical Journal, 55(6), pp. 1507-1515. doi:10.3349/ymj.2014.55.6.1507.

4. Elkind, M.S.V., Tai, W., Coates, K., Paik, M.C. and Sacco, R.L. (2009) 'High-sensitivity C-reactive protein and lipoprotein-associated phospholipase A2 stability before and after stroke and myocardial infarction', Stroke, 40(10), pp. 3233-3237. doi:10.1161/STROKEAHA.109.552802.

5. Jordan, J.E., Montalto, M.C. and Stahl, G.L. (2001) 'Inhibition of mannose-binding lectin reduces postischemic myocardial reperfusion injury', Circulation, 104(12), pp. 1413-1418. doi:10.1161/hc3601.095578.

6. Walsh, M.C., Bourcier, T., Takahashi, K., Shi, L., Busche, M.N., Rother, R.P., Solomon, S.D., Ezekowitz, R.A.B. and Stahl, G.L. (2005) 'Mannose-binding lectin is a regulator of inflammation that accompanies myocardial ischemia and reperfusion injury', Journal of Immunology, 175(1), pp. 541-546. doi:10.4049/jimmunol.175.1.541.

7. Busche, M.N., Pavlov, V., Takahashi, K. and Stahl, G.L. (2009) 'Myocardial ischemia and reperfusion injury is dependent on both IgM and mannose-binding lectin', American Journal of Physiology-Heart and Circulatory Physiology, 297(5), pp. H1853-H1859. doi:10.1152/ajpheart.00049.2009.

8. da Rosa, J.M., Lidani, K.C.F., Andrade, F.A., Sena, L., Nisihara, R., Ambrosio, A.R. and Messias-Reason, I.J. (2024) 'Mannose binding lectin and C3 serum levels in coronary artery disease: a cross-sectional study', Immunological Investigations, 53(5), pp. 752-765. doi:10.1080/08820139.2024.2337023.