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Diagnostic Value of H-FABP, PCT, Lp-PLA2, and Cytokines in Acute Myocardial Infarction

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ABSTRACT

Background & Objective: Myocardial infarction (MI) is one of the highest leading causes of death worldwide. Many biomarkers are universally accepted in clinical practice as crucial diagnostic biomarkers in acute MI. The current study aims to introduce new sensitivity biomarkers to aid the diagnosis and to facilitate faster decision-making in the emergency department.

Materials & Methods: A total of 50 patients, diagnosed with acute myocardial infarction, in Nasiriyah Heart Center, and 30 age-matched healthy individuals were studied. Serum Cardiac Troponin I (cTnI), Myoglobin (MYO), Creatine kinase (CK-MB), Procalcitonin (PCT), Heart-type fatty acid binding protein (H-FABP), Lipoprotein-associated phospholipase A2 (Lp-PLA2), High sensitive C reactive protein (hsCRP), were determined by electro-chemiluminescence immunoassay. Blood sugar and serum total cholesterol, triglycerides, LDL, VLDL, and HDL were determined by using Cobas C311 photometric assays. Serum IL-6 was assayed by electro-chemiluminescence immunoassay, while, IL-9, IL-1β, and TNF-α were assayed by ELISA.

Results: In comparison with healthy control, patients with acute MI showed significant elevation of the serum levels of cTnI, CK-MB, MYO, CRP, H- FABP, PCT, TNF-α, IL-1β, IL-9, and IL-6.

Conclusion: The present study suggests that, in addition to cTnI, CK-MB, and MYO, many other mediators such as CRP, H-FABP, PCT, and cytokines are sensitive to the diagnosis of MI. Furthermore, using human monoclonal antibodies that selectively neutralize cytokines may provide additional insight into cytokines-targeted therapies.

Keywords: CK-MB, CRP, H-FABP, IL-6, Lp-PLA2MI, Myoglobin, PCT, Troponin

Introduction

Myocardial infarction is one of the leading causes of death worldwide. Early diagnosis and management are essential to decrease mortality and morbidity. In clinical practice, many biomarkers are commonly accepted as being essential diagnostic markers of acute MI. However, the early detection of acute MI remains problematic. The development of newer, high-sensitivity assays will create new diagnostic and confirmative tools and facilitate faster decision-making in the emergency department. The American College of Cardiology stated that Troponin I (cTnI) and Creatine kinase (CK-MB), are the marker of choice in diagnosis (1). The elevated cTnI levels are recorded in a high percentage of patients with acute coronary syndromes, even in the absence of elevated CK-MB levels (2). CK-MB is a form of creatine kinase enzyme found primarily in myocardial cells. It is a cardiac biomarker used in the diagnosis of acute MI, myocardial ischemia, or myocarditis (3). CK–MB isoenzyme level, within 24 hours of the onset of the symptoms, has a 98% predictive value for myocardial necrosis (4). Myoglobin (MYO) is a haem protein, present in the cytoplasm of the myocardium and skeletal muscle cells; its plasma concentration is increased 2–3 h post-myocardial ischemic injury (3, 5). The National Academy of Clinical Biochemistry and the American College of Cardiology recommend the use of plasma MYO as an early biomarker of myocardial injury (6).

Many clinical trials indicated that hs-CRP is a risk factor and biomarker with a high predictive value in coronary vascular disease (7-11). H-FABP is a soluble, low molecular-weight protein that is abundant in the cytoplasm of cardiomyocytes. It is one of the biological markers that is early and rapidly released into circulation

post-myocardial damage (12). Lp-PLA2 is an enzyme that hydrolyzes oxidized phospholipids. Several pieces of evidence suggested that Lp-PLA2 promoted atherosclerosis by several pathways. Lp-PLA2 concentration in the plasma was significantly elevated in patients with acute myocardial infarction and stable angina pectoris (13, 14). Procalcitonin (PCT), is extremely elevated in patients with severe bacterial infection. It rapidly responded to many stimuli and bacterial toxins and elevated within 2-3 h. It is highly increased in MI and represents an early new biomarker for the diagnosis and guiding the treatment of patients with MI (15). Numerous studies showed that inflammatory cytokines markedly predict MI. Inflammatory cytokines are believed to be part of the pathophysiology of atherosclerosis development. Recently, it was recorded that increasing cytokines promoted the expression of the proatherogenic gene, and stimulated the inflammatory process in the vessel wall. The secretion of cytokines was increased and their expression was accelerated in MI (16-18).

The study aims to examine the efficacy and diagnostic values of many biomarkers in patients with myocardial infarction in comparison with routinely used markers, (MYO, cTnI, and CK-MB). The establishment of new and sensitivity tests will promote the diagnostic abilities to facilitate fast decisions in the emergency units.

Materials and Methods

This study was a prospective case-control study, carried out on 50 patients diagnosed with acute myocardial infarction (34 males, and 16 females), who visited Heart Hospital in Nasiriyah, Iraq, throughout the period from May 2022 to December 2022, and 30 age-matched healthy subjects as a control group (20 males and, 10 females). The diagnosis was made by a cardiologist. Patients with immunosuppression, malignancy, autoimmune and inflammatory disease, and those with statin therapy were not included in the study, to avoid interference with the studied parameters. Blood samples (10 mL) were drawn by vein puncture as soon as possible after the patient had arrived at the emergency department and diagnosed by the cardiologist as MI. CRP hs, H-FABP, CK-MB, Trop I, MYO, Lp-PLA2 and A2, and PCT were determined by electro-chemiluminescence immunoassay (Nipigon Health Corp., Canada). Electrochemiluminescence immunoassay (ECLIA) is a quantitative method used to measure biomarkers based on the change in electrochemiluminescence (ECL) signal before and after immunoreaction. The test was performed for each biomarker according to the operational manuals of the manufacturing company. Blood sugar (Randox, United Kingdom) and serum total cholesterol, triglycerides (Biolabo /France), LDL, VLDL, and HDL (Cobas /Germany) were determined by using Cobas C311 photometric assays. Serum IL-6 was determined by electro-chemiluminescence immunoassay, while, IL-9, IL-1β and TNF-α were assayed by Enzyme-linked immunoassay (ELISA). ELISA is used to study specific antibodies binding the target antigen and detecting the quantity of antigens binding. The test was carried out for each parameter according to the operational manuals of the manufacturing company.

The ethical committee at Thi-Qar Health Directorate has approved the research, and informed consent was taken from all participants.

The statistical significance was determined using the student t-test by SPSS, version 26 (SPSS Inc., Chicago, IL., USA).

Results

Patients with myocardial infarction showed normal random blood sugar (102.6±30.2 vs 98.0±26.2), significantly declined HDL-C (39.8±2.7 vs. 44.7±3.2) and significantly elevated levels of total cholesterol (162.5±9.2 vs. 149.8±8.6), triglycerides (151.3±10.4 vs. 121.9±15.2), LDL (85.9±2.2 vs. 79.8±8.2) and VLDL (32.1±3.9 vs. 24.4±2.9) in comparison with healthy subjects of the same age group (Table 1).

In comparison with healthy control, patients with acute MI also showed significant elevation of the serum levels of cTnI (0.36±0.002 vs. 0.02±0.00), CK-MB (2.67±0.09 vs. 1.8±0.06 ng/mL), MYO (68.2±6.1 vs. 59.4±8.4 ng/mL), CRP (92.7±4.2 vs. 15.1±1.1 nmol/L), H- FABP (7.16±1.3 vs. 4.9±0.6 ng/mL), and PCT (0.048±0.013 vs. 0.012±0.004 ng/mL). However, the serum level of Lp-PLA2 didn't significantly change in MI in comparison with healthy control (Table 2).

Furthermore, the patients of MI revealed significantly higher serum levels of IL-6 (7.255±3.81 vs. 4.48±1.98 Pg/mL, $P<0.05$), IL-9 (5.21±0.84 vs. 1.98±0.42 Pg/mL, $P<0.05$), IL1β (20.11±3.53 vs. 11.71±2.11 nmol/L, $P<0.01$) and TNF-α) 17.97±2.82 vs. 8.19±1.82 ng/mL, $P<0.01$) compared with healthy control (Table 3).

Table 1. Random blood sugar and lipid profile in patients with acute MI in comparison with healthy control.

Groups	Age	RBS mg/dL	TC mg/dL	TG mg/dL	LDL-C mg/dL	VLDL-C mg/dL	HDL-C mg/dL
Healthy control	30.2±3.2 [a]	98.0±26.2 [a]	149.8±8.6[a]	121.9±15.2[a]	79.8±8.2[a]	24.4±2.9[a]	44.7±3.2[a]
MI patients	29.1±4.1 [a]	102.6±30.2 [a]	162.5±9.2[b]	151.3±10.4[b]	85.9±2.2 [b]	32.1±3.9[b]	39.8±2.7[b]

Vertically, a similar letter means not significant.

HDL-C: high-density lipoprotein cholesterol, LDL-C: low-density lipoprotein cholesterol, RBS: Random blood sugar, TC: total cholesterol, TG: triglycerides, VLDL-C: very low-density lipoprotein cholesterol.

Table 2. The levels of biomarkers in the patients with MI compared with healthy control.

Groups	CRP nmol/L	H- FABP ng/mL	CK-MB ng/mL	cTnI ng/mL	MYO ng/mL	Lp-PLA2 ng/mL	PCT ng/mL
Healthy control	15.1±1.1 [a]	4.9± 0.6[a]	1.8±0.06[a]	0.02±0.00 [a]	59.4±8.4[a]	132.9±6.2 [a]	0.012±0.004[a]
MI patients	92.7± 4.2 [b]	7.16±1.3 [b]	2.67±0.09 [b]	0.36±0.002 [b]	68.2±6.1[b]	128.2±5.4 [a]	0.048± 0.013 [b]

Vertically, a similar letter means not significant.
CK-MB: Creatine kinase, CRP hs: Highly sensitive C reactive protein, H-FABP: heart-type fatty acid binding protein, IL6: Interleukin 6, Lp-PLA2: Lipoprotein-associated phospholipase A2, MYO: Myoglobin, PCT: Procalcitonin, cTnI: Cardiac Troponin I.

Table 3. Serum cytokines levels in patients with MI in comparison with the healthy control group.

Cytokines	Healthy control	MI patients	P-value
IL-6 (Pg/mL)	4.48±1.98	7.255±3.81	<0.05
IL-9 (Pg/mL)	1.98±0.42	5.21±0.84	<0.05
IL1β (nmol/L)	11.71±2.11	20.11±3.53	<0.01
TNF-α (ng/mL)	8.19±1.82	17.97±2.82	<0.01

Discussion

The current study revealed that patients with acute MI showed significantly elevated levels of cTnI, CK-MB, and MYO. American College of Cardiology and the European Society of Cardiology stated that cTnI and CK-MB were the biomarkers of choice in the diagnosis of MI (9). The elevation of cTnI levels was recorded in a high percentage of acute MI patients, even in the absence of elevated CK-MB levels (2). CK-MB is a cardiac marker used to confirm the diagnosis of acute MI (3). CK–MB determination, within 24 hours of the onset of the symptoms, has a 98% predictive value for myocardial necrosis (4). MYO is rapidly released into the blood; it elevated within 2–3 h post-MI (3, 5, 19). It was also recommended as an early biomarker of myocardial damage (6).

Our study also showed that patients with acute MI showed significantly elevated levels of serum H-FABP. H-FABP is a sensitive early biomarker, it is elevated 1 h post-AMI (20). It appears that the diagnostic value of H-FABP is much higher than other AMI diagnostic biomarkers (21). H-FABP showed significantly superior sensitivity than cTnI, MYO, and CK-MB, in those with suspected AMI before hospitalization (22).

Furthermore, CRP was also significantly elevated in patients with acute MI in our study, CRP was known as an acute phase protein, and many authors classified CRP as a clinical predictor of MI (23-25). CRP promotes the proliferation and migration of endothelial cells, potentiates the complement system and is involved in the pathogenesis of atherosclerosis (26-28).

The patients with acute MI also showed significantly elevated serum levels of PCT. High serum PCT level is associated with a great degree of inflammation. Thus, the extensive arteriosclerotic plaques are also reflected by higher PCT serum levels. Serum levels in the range of 0.06 to 3 ng/mL indicated arteriosclerosis and represented a valuable diagnostic index, of acute myocardial infarction (15). Like CRP, PCT is not specific and only plays a supplemental role in the cardiovascular system (15, 29).

However, the current study didn't show significant changes in Lp-PLA2 in acute MI. Lp-PLA2 is the enzyme that is produced mostly by neutrophils and macrophages from atherosclerotic plaques, and after that conveyed to the bloodstream via HDL-C as well as LDL-C (30, 31). It is an important biomarker of inflammation (13). In clinical trial using an Lp-PLA2 inhibitor, showed no benefit in MI patients as a preventive treatment (32). Data analysis revealed that Lp-PLA2 didn't participate in the pathophysiology of atherosclerosis (33).

Recently, there has been a lot of pieces of evidence proving that inflammation plays a pivotal role in pathophysiology (34). The current research showed that IL-6 was significantly elevated in MI patients. Many previous studies mentioned that IL-6 and soluble IL-6 receptors were increased in acute myocardial infarction, and the IL-6 level was proportional to infarction size and the decline in left ventricular ejection fraction (35-37). IL-6 induced LDL-receptor expression on the macrophage's surface and promoted LDL uptake by macrophage, therefore, accelerating

lipid deposition and enhancing foam cell formation (38). It increased matrix metalloproteinase synthesis, degraded the extracellular matrix, and increased the susceptibility of the plaques to rupture (39, 40). IL-6 was also important in cardiac fibroblasts by transiently inducing a hyaluronan-rich matrix that in turn promoted the inflammatory responses, and myofibroblastic phenotype, and initiated the cardio-protective program after AMI (41). Furthermore, the loss of viable myocardium after MI was linked to an inflammatory response. A clinical trial showed that myocardial salvage in patients with acute MI was increased by tocilizumab, which is attached to the IL-6 receptor and inhibited IL-6 signaling (42), and myocardial salvage in patients with acute STEMI was increased by Tocilizumab. Microvascular obstruction was less extensive in the tocilizumab group (43).

Our study also revealed that IL-9 was significantly increased in MI patients. According to previous studies, IL-9 level was increased in different atherosclerotic disorders both systemically and locally in the lesion, in addition to elevation of IL-9 and IL-9R expression, which suggested a role for the IL-9/IL-9R axis in the atherosclerotic process (44, 45). Elevated circulated IL-9 promoted $CD8^+$ T-cell cytotoxicity in AMI patients. The enhancement of $CD8^+$ T-cell cytotoxicity induced by $CD4^+$ $CCR4^-$ $CCR6^-$ $CXCR3^-$ cells was IL-9 dependent. According to these results, it was suggested that IL-9-secreting $CD4^+$ T cells contributed to the pathogenesis of AMI through enhancement of $CD8^+$ T-cell cytotoxicity (44).

The significant increase in the level of IL-1β in patients with MI in this study was in line with many other authors. Many studies have suggested that IL-1β was involved in the pathogenesis of atherosclerosis (34, 46-49). Canakinumab, the human monoclonal antibody that selectively neutralizes IL-1β, improved cardiovascular outcomes and prevented the recurrence of cardiovascular events, which provided additional insight into IL-1β-targeted therapies (46-49).

TNF-α was also significantly elevated in MI patients in our study. Previously also recorded that TNF-α was significantly elevated in patients with acute coronary events when the samples of the blood were taken after the occurrence of MI (50-52). The level of TNF-α and its gene expression and subsequently its signaling pathways are changed at different points of the MI pathophysiological process (53). The proatherogenic effects of TNF-α on the endothelium may be attributed to a decrease in the bioavailability of NO, stimulation of vascular superoxide production, decrease of Ca^{2+} uptake by the sarcoplasmic reticulum, decrease of myofilament Ca^{2+} sensitivity, increasing the infiltration of the endothelium by inflammatory cells and inducing of left ventricular dysfunction (54) Furthermore, administration of TNF-α inhibitor during the first week of myocardial infarction reduced the inflammatory cytokines and the infiltration of the inflammatory cells in and around the infarct area (55). Accordingly, serum level of TNF-α was recommended as markers in acute STEMI to follow up the worsening of left ventricular systolic functions, and heart failure (56).

Conclusion

Early diagnosis remains the essential principle in the treatment of MI and still needs sensitive diagnostic biomarkers. The present study suggests that in addition to cTnI, CK-MB, and MYO, many other mediators such as CRP, H-FABP, PCT, and cytokines are sensitive, to serve as good indicators for diagnosis of MI and enable clinicians to monitor the cases of MI promptly and develop methods to decrease the adverse post-ischemic effects.

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Author Contributions

Amer Muayad Hussein carried out the laboratory investigation. Ernez Hajri Samia and Al-Snafi Ali Esmail participate in opinion, designing, supervision, interpretation, discussion and drafting the manuscript.

Ethics approval

The ethical committee at Thi-Qar Health Directorate (2022161 in 31 /5/ 2022) has approved the research, and an informed consents was taken from all participants. All methods were performed in accordance with the local guidelines and regulations of Ibn El Jazzar Faculty of Medicine, University of Sousse, Sousse, Tunisia and Thi Qar Health directorate.

Abbreviations

CK-MB: Creatine kinase, CRP hs: High sensitive C reactive protein, cTnI: Cardiac Troponin I, HDL-C: high-density lipoprotein cholesterol, H-FABP: heart-type fatty acid binding protein, IL6: Interleukin 6, LDL-C: low-density lipoprotein cholesterol, Lp-PLA2: Lipoprotein-associated phospholipase A2, MI: Myocardial infarction, MYO: Myoglobin, PCT: Procalcitonin, BS: blood sugar, TC: total cholesterol, TG: triglycerides, VLDL-C: very low-density lipoprotein cholesterol.

Conflict of Interest

The authors declare no conflicts of interest.

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References

1. Luciano B, Allan SJ. Troponin: the biomarker of choice for the detection of cardiac injury. Can Med Assoc J. 2005;173(10):1191. [DOI:10.1503/cmaj/051291]
2. Ottani F, Galvani M, Nicolini FA, Ferrini D, Pozzati A, Di Pasquale G, et al. Elevated cardiac troponin levels predict the risk of adverse outcome in patients with acute coronary syndromes. Am Heart J. 2000;140(6):917-27. [DOI:10.1067/mhj.2000.111107] [PMID]
3. Kemp M, Donovan J, Higham H, Hooper J. Biochemical markers of myocardial injury. Br J Anaesth. 2004;93(1):63-73. [DOI:10.1093/bja/aeh148] [PMID]
4. Antman E, Bassand J-P, Klein W, Ohman M, Lopez Sendon JL, Rydén L, et al. Myocardial infarction redefined-a consensus document of the Joint European Society of Cardiology/American College of Cardiology committee for the redefinition of myocardial infarction: the Joint European Society of Cardiology/American College of Cardiology Committee. Journal of the American College of Cardiology. 2000;36(3):959-69. [DOI:10.1016/S0735-1097(00)00804-4] [PMID]
5. Asl SK, Rahimzadegan M. The recent progress in the early diagnosis of acute myocardial infarction based on myoglobin biomarker: Nano-aptasensors approaches. J Pharm Biomed Anal. 2022;211: 114624. [DOI:10.1016/j.jpba.2022.114624] [PMID]
6. Collinson PO, Stubbs PJ, Kessler AC. Multicentre evaluation of the diagnostic value of cardiac troponin T, CK-MB mass, and myoglobin for assessing patients with suspected acute coronary syndromes in routine clinical practice. Heart. 2003;89(3):280. [DOI:10.1136/heart.89.3.280] [PMID] [PMCID]
7. Danesh J, Whincup P, Walker M, Lennon L, Thomson A, Appleby P, et al. Low grade inflammation and coronary heart disease: prospective study and updated meta-analyses. BMJ. 2000;321(7255):199. [PMID] [PMCID] [DOI:10.1136/bmj.321.7255.199]
8. Ridker PM, Hennekens CH, Buring JE, Rifai N. C-Reactive Protein and Other Markers of Inflammation in the Prediction of Cardiovascular Disease in Women. N Engl J Med. 2000;342(12): 836-43. [DOI:10.1056/NEJM200003233421202] [PMID]
9. Ridker Paul M. C-Reactive Protein and the Prediction of Cardiovascular Events Among Those at Intermediate Risk. J Am Coll Cardiol. 2007;49(21):2129-38. [DOI:10.1016/j.jacc.2007.02.052] [PMID]
10. Ridker PM, Rifai N, Rose L, Buring JE, Cook NR. Comparison of C-Reactive Protein and Low-Density Lipoprotein Cholesterol Levels in the Prediction of First Cardiovascular Events. N Engl J Med. 2002;347(20):1557-65. [DOI:10.1056/NEJMoa021993] [PMID]
11. Shah PK. Circulating markers of inflammation for vascular risk prediction: are they ready for prime time. Am Heart Assoc; 2000:1758-9. [DOI:10.1161/01.CIR.101.15.1758] [PMID]
12. Bertinchant JP, Polge A. [Diagnostic and prognostic value of heart-type fatty acid-binding protein (H-FABP), an early biochemical marker of myocardial injury]. Arch Mal Coeur Vaiss. 2005; 98(12):1225-31.
13. Yang L, Liu Y, Wang S, Liu T, Cong H. Association between Lp-PLA2 and coronary heart disease in Chinese patients. J Int Med Res. 2017; 45(1):159-69. [DOI:10.1177/0300060516678145] [PMID] [PMCID]
14. Epps KC, Wilensky RL. Lp-PLA2- a novel risk factor for high-risk coronary and carotid artery disease. J Intern Med. 2011;269(1):94-106. [DOI:10.1111/j.1365-2796.2010.02297.x][PMID]
15. Arneth B. High-Sensitivity Procalcitonin (hs-PCT): A Marker for Identification of Arteriosclerosis and Myocardial Infarction? Lab Med. 2008;39(10):607-10. [DOI:10.1309/LM6E5BJZ2TQSCGHZ]
16. Kamimura D, Ishihara K, Hirano T. IL-6 signal transduction and its physiological roles: the signal orchestration model. Rev Physiol Biochem Pharmacol. 2004:1-38. [PMID] [DOI:10.1007/s10254-003-0012-2]
17. Tedgui A, Mallat Z. Cytokines in Atherosclerosis: Pathogenic and Regulatory Pathways. Physiol Rev. 2006;86(2):515-81. [DOI:10.1152/physrev.00024.2005] [PMID]
18. Harker JA, Lewis GM, Mack L, Zuniga EI. Late Interleukin-6 Escalates T Follicular Helper Cell Responses and Controls a Chronic Viral Infection. Science. 2011;334(6057):825-9. [PMID][PMCID] [DOI:10.1126/science.1208421]
19. Woo J, Lacbawan FL, Sunheimer R, Lefever D, McCabe JB. Is Myoglobin Useful in the Diagnosis of Acute Myocardial Infarction in the Emergency Department Setting? Am J Clin Pathol. 1995; 103(6):725-9. [DOI:10.1093/ajcp/103.6.725] [PMID]

20. Kleine AH, Glatz JFC, Van Nieuwenhoven FA, Van der Vusse GJ. Release of heart fatty acid-binding protein into plasma after acute myocardial infarction in man. Lipid Metabolism in the Healthy and Disease Heart. 1992. p. 155-62. [DOI:10.1007/978-1-4615-3514-0_22]

21. Ishii J, Wang J-h, Naruse H, Taga S, Kinoshita M, Kurokawa H, et al. Serum concentrations of myoglobin vs human heart-type cytoplasmic fatty acid-binding protein in early detection of acute myocardial infarction. Clin Chem. 1997;43(8): 1372-8. [DOI:10.1093/clinchem/43.8.1372] [PMID]

22. Ecollan P, Collet J-P, Boon G, Tanguy M-L, Fievet M-L, Haas R, et al. Pre-hospital detection of acute myocardial infarction with ultra-rapid human fatty acid-binding protein (H-FABP) immunoassay. Int J Cardiol. 2007;119(3):349-54. [DOI:10.1016/j.ijcard.2006.09.003] [PMID]

23. Yousuf O, Mohanty BD, Martin SS, Joshi PH, Blaha MJ, Nasir K, et al. High-sensitivity C-reactive protein and cardiovascular disease: a resolute belief or an elusive link? J Am Coll Cardiol. 2013;62(5):397-408. [DOI:10.1016/j.jacc.2013.05.016] [PMID]

24. Bielas H, Meister-Langraf RE, Schmid J-P, Barth J, Znoj H, Schnyder U, et al. C-reactive protein as a predictor of posttraumatic stress induced by acute myocardial infarction. Gen Hosp Psychiatry. 2018;53:125-30. [PMID] [DOI:10.1016/j.genhosppsych.2018.03.008]

25. Best LG, Zhang Y, Lee ET, Yeh J-L, Cowan L, Palmieri V, et al. C-Reactive Protein as a Predictor of Cardiovascular Risk in a Population With a High Prevalence of Diabetes. Circulation. 2005; 112(9):1289-95. [DOI:10.1161/CIRCULATIONAHA.104.489260] [PMID]

26. Liu N, Liu J, Ji Y, Lu P, Wang C, Guo F. C-Reactive Protein Induces TNF-α Secretion by p38 MAPK-TLR4 Signal Pathway in Rat Vascular Smooth Muscle Cells. Inflammation. 2011;34(4): 283-90. [DOI:10.1007/s10753-010-9234-z] [PMID]

27. Cermak J, Key NS, Bach RR, Balla J, Jacob HS, Vercellotti GM. C-reactive protein induces human peripheral blood monocytes to synthesize tissue factor. Blood. 1993;82(2):513-20. [PMID] [DOI:10.1182/blood.V82.2.513.bloodjournal822513] [DOI:10.1182/blood.V82.2.513.513]

28. Devaraj S, Kumaresan PR, Jialal I. Effect of C-reactive protein on chemokine expression in human aortic endothelial cells. J Mol Cell Cardiol. 2004;36(3):405-10. [DOI:10.1016/j.yjmcc.2003.12.005] [PMID]

29. Sun S, Wang F, Yu M, Kang J. Clinical study of serum procalcitonin level in patients with myocardial infarction complicated by pulmonary infection. Exp Ther Med. 2018;16(6):5210-4. [DOI:10.3892/etm.2018.6841] [PMID] [PMCID]

30. Macphee CH, Nelson J, Zalewski A. Role of lipoprotein-associated phospholipase A2 in atherosclerosis and its potential as a therapeutic target. Curr Opin Pharmacol. 2006;6(2):154-61. [DOI:10.1016/j.coph.2005.11.008] [PMID]

31. Zalewski A, Macphee C. Role of lipoprotein-associated phospholipase A2 in atherosclerosis: biology, epidemiology, and possible therapeutic target. Arteriosclerosis, thrombosis, and vascular biology. 2005;25(5):923-31. [PMID] [DOI:10.1161/01.ATV.0000160551.21962.a7]

32. O'Donoghue ML, Braunwald E, White HD, Steen DL, Lukas MA, Tarka E, et al. Effect of darapladib on major coronary events after an acute coronary syndrome: the SOLID-TIMI 52 randomized clinical trial. Jama. 2014;312(10):1006-15. [DOI:10.1001/jama.2014.11061] [PMID]

33. Ueshima H, Kadowaki T, Hisamatsu T, Fujiyoshi A, Miura K, Ohkubo T, et al. Lipoprotein-associated phospholipase A2 is related to risk of subclinical atherosclerosis but is not supported by Mendelian randomization analysis in a general Japanese population. Atherosclerosis. 2016;246: 141-7. [PMID] [DOI:10.1016/j.atherosclerosis.2015.12.027]

34. Moriya J. Critical roles of inflammation in atherosclerosis. J Cardiol. 2019;73(1):22-7. [DOI:10.1016/j.jjcc.2018.05.010] [PMID]

35. Tøllefsen IM, Shetelig C, Seljeflot I, Eritsland J, Hoffmann P, Andersen GØ. High levels of interleukin-6 are associated with final infarct size and adverse clinical events in patients with STEMI. Open Heart. 2021;8(2):e001869. [PMID] [DOI:10.1136/openhrt-2021-001869] [PMCID]

36. Anderson DR, Poterucha JT, Mikuls TR, Duryee MJ, Garvin RP, Klassen LW, et al. IL-6 and its receptors in coronary artery disease and acute myocardial infarction. Cytokine. 2013;62(3):395-400. [DOI:10.1016/j.cyto.2013.03.020] [PMID]

37. Su J-H, Luo M-Y, Liang N, Gong S-X, Chen W, Huang W-Q, et al. Interleukin-6: a novel target for cardio-cerebrovascular diseases. Front Pharmacol. 2021;12:745061. [PMID] [PMCID] [DOI:10.3389/fphar.2021.745061]

38. Schuett H, Luchtefeld M, Grothusen C, Grote K, Schieffer B. How much is too much? Interleukin-6 and its signalling in atherosclerosis. J Thromb Haemost. 2009;102(08):215-22. [DOI:10.1160/TH09-05-0297] [PMID]

39. Suzuki H, Kusuyama T, Sato R, Yokota Y, Tsunoda F, Sato T, et al. Elevation of matrix

metalloproteinases and interleukin-6 in the culprit coronary artery of myocardial infarction. Eur J Clin Invest. 2008;38(3):166-73. [PMID] [DOI:10.1111/j.1365-2362.2007.01919.x]

40. Madan M, Bishayi B, Hoge M, Amar S. Atheroprotective role of interleukin-6 in diet- and/or pathogen-associated atherosclerosis using an ApoE heterozygote murine model. Atherosclerosis. 2008;197(2):504-14. [DOI:10.1016/j.atherosclerosis.2007.02.023] [PMID] [PMCID]

41. Müller J, Gorressen S, Grandoch M, Feldmann K, Kretschmer I, Lehr S, et al. Interleukin-6-dependent phenotypic modulation of cardiac fibroblasts after acute myocardial infarction. Basic Res Cardiol. 2014;109(6):440. [DOI:10.1007/s00395-014-0440-y] [PMID]

42. Fernández-Ruiz I. Early inhibition of IL-6 signalling after an acute MI improves myocardial salvage. Nat Rev Cardiol. 2021;18(7):460. [DOI:10.1038/s41569-021-00560-1] [PMID]

43. Broch K, Anstensrud Anne K, Woxholt S, Sharma K, Tøllefsen Ingvild M, Bendz B, et al. Randomized Trial of Interleukin-6 Receptor Inhibition in Patients With Acute ST-Segment Elevation Myocardial Infarction. J Am Coll Cardiol. 2021;77(15):1845-55. [DOI:10.1016/j.jacc.2021.02.049] [PMID]

44. Gang H, Peng D, Hu Y, Tang S, Li S, Huang Q. Interleukin-9-secreting CD4+ T cells regulate CD8+ T cells cytotoxicity in patients with acute coronary syndromes. Apmis. 2021;129(2):91-102. [DOI:10.1111/apm.13094] [PMID]

45. Gregersen I, Skjelland M, Holm S, Holven KB, Krogh-Sørensen K, Russell D, et al. Increased systemic and local interleukin 9 levels in patients with carotid and coronary atherosclerosis. PLoS One. 2013;8(8):e72769. [PMID] [PMCID] [DOI:10.1371/journal.pone.0072769]

46. Ridker PM, MacFadyen JG, Thuren T, Everett BM, Libby P, Glynn RJ, et al. Effect of interleukin-1β inhibition with canakinumab on incident lung cancer in patients with atherosclerosis: exploratory results from a randomised, double-blind, placebo-controlled trial. The Lancet. 2017;390(10105):1833-42. [DOI:10.1016/S0140-6736(17)32247-X] [PMID]

47. Ridker PM, Howard CP, Walter V, Everett B, Libby P, Hensen J, et al. Effects of Interleukin-1β Inhibition With Canakinumab on Hemoglobin A1c, Lipids, C-Reactive Protein, Interleukin-6, and Fibrinogen. Circulation. 2012;126(23):2739-48.[DOI:10.1161/CIRCULATIONAHA.112.122556] [PMID]

48. Ridker PM, Thuren T, Zalewski A, Libby P. Interleukin-1β inhibition and the prevention of recurrent cardiovascular events: rationale and design of the Canakinumab Anti-inflammatory Thrombosis Outcomes Study (CANTOS). Am Heart J. 2011;162(4):597-605. [DOI:10.1016/j.ahj.2011.06.012] [PMID]

49. Ridker PM, Everett BM, Thuren T, MacFadyen JG, Chang WH, Ballantyne C, et al. Antiinflammatory therapy with canakinumab for atherosclerotic disease. N Engl J Med. 2017; 377(12):1119-31. [DOI:10.1056/NEJMoa1707914] [PMID]

50. Mizia-Stec K, Gasior Z, Zahorska-Markiewicz B, Janowska J, Szulc A, Jastrzebska-Maj E, et al. Serum tumour necrosis factor-α, interleukin-2 and interleukin-10 activation in stable angina and acute coronary syndromes. Coron Artery Dis. 2003;14(6):431-8. [PMID] [DOI:10.1097/00019501-200309000-00003]

51. Ridker PM, Rifai N, Pfeffer M, Sacks F, Lepage S, Braunwald E. Elevation of tumor necrosis factor-α and increased risk of recurrent coronary events after myocardial infarction. Circulation. 2000;101(18):2149-53. [DOI:10.1161/01.CIR.101.18.2149] [PMID]

52. Martins TB, Anderson JL, Muhlestein JB, Horne BD, Carlquist JF, Roberts WL, et al. Risk Factor Analysis of Plasma Cytokines in Patients With Coronary Artery Disease by a Multiplexed Fluorescent Immunoassay. Am J Clin Pathol. 2006;125(6):906-13. [DOI:10.1309/Q3E6KF0QD3U3YL6T] [PMID]

53. Tian M, Yuan Y-C, Li J-Y, Gionfriddo MR, Huang R-C. Tumor necrosis factor-α and its role as a mediator in myocardial infarction: A brief review. Chronic Dis Transl Med. 2015;1(1):18-26. [DOI:10.1016/j.cdtm.2015.02.002] [PMID] [PMCID]

54. Sack MN. Tumor necrosis factor-α in cardiovascular biology and the potential role for anti-tumor necrosis factor-α therapy in heart disease. Pharmacol Ther. 2002;94(1):123-35. [DOI:10.1016/S0163-7258(02)00176-6] [PMID]

55. Wang X, Guo Z, Ding Z, Mehta JL. Inflammation, Autophagy, and Apoptosis After Myocardial Infarction. J Am Heart Assoc. 2023;7(9):e008024. [DOI:10.1161/JAHA.117.008024] [PMID] [PMCID]

56. Mahmoud AH, Taha NM, Zakhary M, Tadros MS. PTEN gene & TNF-alpha in acute myocardial infarction. IJC Heart & Vasculature. 2019;23: 100366. [DOI:10.1016/j.ijcha.2019.100366] [PMID] [PMCID]

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