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BIOMARKERS IN ACUTE MYOCARDIAL INFARCTION

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INTRODUCTION

Acute myocardial infarction (AMI) is a leading global cause of mortality. Conducting thorough risk assessments for chest pain patients and minimizing unfavorable outcomes can reduce morbidity, mortality, improve patient quality of life, and lower healthcare costs in various nations. In contemporary cardiology, multiple biomarkers are employed for diagnosis of myocardial infarction.

Biomarkers play a pivotal role in the diagnosis and management of acute myocardial infarction (AMI). They are measurable indicators that provide valuable information about the presence, extent, and severity of cardiac injury. Commonly used biomarkers in AMI include cardiac troponins, creatine kinase-MB (CK-MB), and myoglobin. These biomarkers assist in the early diagnosis, risk stratification, and monitoring of AMI patients, ultimately aiding in timely and effective medical intervention to improve patient outcomes.

Given the critical importance of timely detection and diagnosis in enhancing survival rates for acute myocardial infarction, cardiac biomarkers play a significant role in the prompt diagnosis of such cases.

CARDIAC BIOMARKERS

1. **Aspartate Aminotransferase (AST)**

   AST was one of the earliest biomarkers used in the diagnosis of acute MI and was considered as an indicator of necrosis in cardiac myocytes[1]. Following an acute MI, the levels of AST rise in 3 to 4 hours. After reaching a peak at 15 to 28 hours, the levels begin to decline becoming normal in 5 days. However, because of their non-specific nature causing elevation in other cardiac, hepatic and pulmonary diseases, their routine use has been largely discontinued and they are only of historical importance today.

2. **Lactate Dehydrogenase (LDH)**

   Lactate dehydrogenase (LDH) was used extensively in the past for the diagnosis of acute MI. But its use in clinical setting is greatly dimished now due to the availability of more sensitive and specific markers. LDH exists in 5 isoenzyme forms, with LDH 1 predominantly being present in cardiac myocytes and erythrocytes while LDH 2 is present predominantly in white blood cells.LDH levels increase 24–72 hours after a myocardial infarction , attains peak concentration in 3–4 days and remains elevated for 8 to 14 days, thereby serving as a late marker for myocardial infarction. The flipped LDH pattern wherein after myocardial infarction, LDH-1 concentration exceeds that of LDH 2 was earlier used in detection of myocardial ischemia. However it was observed that this phenomemnon also occurred during hemolysis. Besides LDH itself is a non specific marker as its concentration is increased in a variety of conditions and is therefore of limited diagnostic value today.The only usage for LDH in the present day with reference to acute MI is to differentiate acute MI from subacute MI when troponin concentration is elevated and CK and CK_MB are normal[2]

3. **Cardiac Troponin**

   Proteins called troponins control how hard muscles contract[3].Cardiac troponin I (cTnI), cardiac troponin T (cTnT), and cardiac troponin C are the subunits found in the myocardium. All three are essential parts of the heart muscle's contractile system. Both cTnI and cTnT have immunoassays available, and either of the troponin can be utilized to look into potential

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myocardial infarction or injury. Since cardiac troponins are specific to myocardial tissue, creatine kinase-MB has been superseded in the investigation of potential myocardial injury.

Prior to a significant increase in cardiac troponin I (cTnI), acute hs-CRP phase levels may prime the body to react to any necrotic or injured tissue[4]. Patients are more hyper responsive to circulating cTnI when they initially present with high HS-CRP titres[5]. The late markers are TnT and TnI. One excellent AMI biomarker during the first 10–12 hours is CK-MB. If CK-MB remains within normal limits, then an elevation in TnI is suggestive of myocardial injury. In terms of AMI diagnosis, TnI is more precise.

4. Myoglobin

Myoglobin, a heme protein found in both cardiac and skeletal muscles, primarily serves to deliver oxygen to muscle tissue. It plays a crucial role as one of the early indicators for diagnosing acute myocardial infarction (AMI) during the early stages. Myoglobin levels exhibit a rapid increase within the first 30 minutes following the onset of an acute cardiac event. Within 6 to 10 hours, myoglobin becomes elevated in all AMI patients and reaches its peak concentration around the 12th hour. Subsequently, myoglobin can be detected in the serum following an AMI[6].

5. Creatinine Kinase

Creatine kinase (CK), previously referred to as creatine phosphokinase, is an enzyme found within the cells. It is highly concentrated in skeletal muscle, myocardium, and the brain. Smaller quantities of this enzyme are also present in various visceral tissues. Cell membrane damage resulting from hypoxia or other injuries causes the release of CK from the intracellular cytosol into the systemic circulation. Elevated levels of CK in the serum have been employed as a sensitive, yet not very specific, diagnostic test for myocardial infarction. The lack of specificity arises from the widespread presence of CK in numerous tissues beyond the myocardium[7].

The enzyme exists in a dimeric form composed of two subunits, M and B, and comprises three isoenzymes: CK-BB (CK1), CK-MB (CK2), and CK-MM (CK3). CK-MM is the prevalent variant present in all tissues. CK-BB is located in the brain, kidney, and gastrointestinal tract, while CK-MB is distributed in the heart, skeletal muscle, small intestine, diaphragm, uterus, tongue, and prostate[7]

In cases of myocardial injury, CK-MB follows a distinctive temporal pattern. Initially, CK-MB levels start to rise gradually, typically within 4 to 9 hours after the onset of chest pain. This increase continues until it reaches its peak concentration, which typically occurs around 24 hours after the initial event. Subsequently, CK-MB levels start to decline, and within 48 to 72 hours, they return to their baseline levels. This progression in CK-MB levels is a significant indicator in the diagnosis and monitoring of myocardial injury[6].

6. Heart-type fatty acid binding protein (H-FABP)

Fatty acid binding proteins (FABPs) constitute a family of proteins tasked with the crucial role of facilitating the movement of fatty acids and lipophilic substances into or out of cells. This family encompasses various types, including heart-type, adipocyte-type, epidermal-type, ileal-type, brain-type, myelin-type, and testis-type FABPs. Notably, heart-type FABP (H-FABP) is primarily localized in the heart and has a molecular weight of 15 kDa[8].

In the event of myocardial injury, there is a rapid and significant increase in serum H-FABP levels, rendering it a valuable marker for detecting myocardial infarction. Furthermore, H-FABP proves to be a valuable prognostic indicator in individuals with proven acute coronary syndrome[9]

7. C - Reactive Protein (CRP)

One member of the pentraxins family of plasma proteins is C-reactive protein (CRP). Since CRP is an acute phase protein that is produced by hepatocytes in response to proinflammatory cytokines, including interleukin-6, it is frequently utilized as a general inflammatory marker[10]. Experiments have shown that CRP may influence the development of CAD by several mechanisms, including activating platelets and the complement system, inhibiting fibrinolysis, encouraging the growth of smooth muscle cells, polarizing microphages, and lipid deposition[11,12]. High sensitivity CRP (HS-CRP) might be a straightforward indicator of the degree of the inflammatory response to myocardial ischemia in the early stages of AMI[13].

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In addition to myocardial necrosis and infarct size, atherosclerotic mass, an underlying inflammatory process, and circulating proinflammatory cytokines are examples of tissue damage that might result in an increase in HS-CRP in STEMI patients[14].There is evidence linking HS-CRP to hospital outcomes, including angina, MI, and mortality. This emphasizes how important this biomarker is for determining a patient's risk when they have an acute coronary syndrome[15]. Following an ST-elevation myocardial infarction (STEMI), there is an initial rise in high sensitivity CRP (HS-CRP) that peaks in 48–72 hours and then progressively falls over the course of the following several weeks to a reference range of less than 10 mg/L.[16,17]

8. Matrix Metallo-Proteinases (MMP)

The extracellular matrix (ECM) of the heart is structurally intact only when endogenous zinc-dependent endopeptidases known as matrix metalloproteinases (MMPs) are present. Tissue inhibitors of metalloproteinases (TIMPs) control these enzymes. In experimental models of AMI, MMP inhibition has been linked to decreased LV dilatation and wall stress. MMPs may degrade myocardial ECM, which could lead to the development of LV dilatation and heart failure. Re-infarction was not linked to TIMP1, or MMP 9, despite their associations with heart failure, cardiovascular death, or both[18]. Following MI, MMP2 is also increased[19], and this is linked to a poor prognosis[20]. MMP3 has a 72-hour peak and plateau levels that are linked to a follow-up decrease in ejection fraction and an increase in LV volume.[21]

While MMP-3 is linked to heart failure and left ventricular remodeling, elevated levels of MMP-14 are linked to an increased risk of MI mortality.

CONCLUSION

Despite the abundance of newly discovered biomarkers, we continue to lack a thorough understanding of the roles and biochemistry of the various peptides involved in the disease process. Based on the available data, it is challenging to make precise inferences about the ways in which a biomarker might influence prognosis. Because they are simple to measure, many studies use major adverse cardiovascular events or death as their endpoints; however, either of these endpoints could be the result of several different pathophysiological processes. Therefore, beyond Troponin, the biomarkers that are currently available have not been able to significantly contribute to our ability to customize our treatment. It would be highly instructive to conduct randomised trials that use biomarkers to change the course of treatment

A multi-marker approach may help with patient prognosis, risk assessment, and diagnosis, according to some data. The biomarkers listed above that are most likely to be incorporated into bedside practice soon are copeptin, GDF-15, NTproBNP, MRproANP, and MRproADM. Personalized treatment is the potential advantage of a multi-marker strategy since every biomarker would assess a distinct aspect of the disease. A panel of tests with multiple markers could then be utilized to develop an algorithm that supports clinical decision-making. But we're a long way off from reaching this end result.

REFERENCES

1. Ladue Js, Wroblewski F, Karmen A. Serum glutamic oxaloacetic transaminase activity in human acute transmural myocardial infarction. Science. 1954 Sep 24;120(3117):497-9.
2. Yun DD, Alpert JS. Acute coronary syndromes. Cardiology. 1997 May-Jun;88(3):223-37
3. Shave R, Baggish A, George K, Wood M, Scharhag J, Whyte G, et al. Exercise-induced cardiac troponin elevation: evidence, mechanisms, and implications. J Am Coll Cardiol 2010;56:169-76. 10.1016/j.jacc.2010.03.037
4. Al Aseri ZA, Habib SS, Marzouk A. Predictive value of high sensitivity C-reactive protein on progression to heart failure occurring after the first myocardial infarction. Vasc Health Risk Manag. 2019;15:221–227. doi: 10.2147/VHRM.S198452.
5. De Servi S, Mariani M, Mariani G, Mazzone A. C-reactive protein increase in unstable coronary disease cause or effect? J Am Coll Cardiol. 2005;46:1496–1502. doi: 10.1016/j.jacc.2005.05.083.
6. Dasgupta A, Wahed A. Cardiac markers. Clinical Chemistry, Immunology and Laboratory Quality Control. 2014;127–44. doi:10.1016/b978-0-12-407821-5.00008-5

7. Cabaniss CD. Creatine Kinase. In: Walker HK, Hall WD, Hurst JW, editors. Clinical Methods: The History, Physical, and Laboratory Examinations. 3rd ed. Boston: Butterworths; 1990. Chapter 32. PMID: 21250193.
8. Ye X, He Y, Wang S, Wong GT, Irwin MG, Xia Z. Heart-type fatty acid binding protein (H-FABP) as a biomarker for acute myocardial injury and long-term post-ischemic prognosis. Acta Pharmacologica Sinica. 2018;39(7):1155–63. doi:10.1038/aps.2018.37
9. Faqi AS. A comprehensive guide to toxicology in Nonclinical Drug Development. Amsterdam: Academic Press is an imprint of Elsevier; 2017.
10. Ristagno G, Fumagalli F, Bottazzi B, et al. Pentraxin 3 in cardiovascular disease. Front Immunol. 2019;10:823. doi: 10.3389/fimmu.2019.00823.
11. Devaraj S, Jialal I. C-reactive protein polarizes human macrophages to an M1 phenotype and inhibits transformation to the M2 phenotype. Arterioscler Thromb Vasc Biol. 2011;31:1397-1402. doi: 10.1161/ATVBAHA.111.225508.
12. Wang SZ, Wu M, Chen KJ, et al. Hawthorn extract alleviates atherosclerosis through regulating inflammation and apoptosis related factors: an experimental study. Chin J Integr Med. 2019;25:108-115. doi: 10.1007/s11655-018-3020-4.
13. Milano SS, Moura Junior OV, et al. C-reactive protein is a predictor of mortality in ST-segment elevation acute myocardial infarction. Int J Cardiovasc Sci. 2019;32:118-124.
14. Kavsak PA, MacRae AR, Newman AM, et al. Elevated C-reactive protein in acute coronary syndrome presentation is an independent predictor of long-term mortality and heart failure. Clin Biochem. 2007;40:326-329. doi: 10.1016/j.clinbiochem.2006.10.025.
15. Zorzi A, Turri R, Zilio F, et al. At-admission risk stratification for in-hospital life-threatening ventricular arrhythmias and death in non-ST elevation myocardial infarction patients. Eur Heart J Acute Cardiovasc Care. 2014;3:304-312. doi: 10.1177/2048872614528796.
16. Osman R, L'Allier PL, Elgharib N, Tardif JC. Critical appraisal of C-reactive protein throughout the spectrum of cardiovascular disease. Vasc Health Risk Manag. 2006;2:221-237. doi: 10.2147/vhrm.2006.2.3.221.
17. Kang DO, Park Y, Seo JH, et al. Time-dependent prognostic effect of high sensitivity C-reactive protein with statin therapy in acute myocardial infarction. J Cardiol. 2019;74:74-83. doi: 10.1016/j.jjcc.2018.12.022.
18. Kelly D, Khan SQ, Thompson M, Cockerill G, Ng LL, Samani N, Squire IB. Plasma tissue inhibitor of metalloproteinase-1 and matrix metalloproteinase-9: novel indicators of left ventricular remodelling and prognosis after acute myocardial infarction. Eur Heart J. 2008.
19. Kelly D, Cockerill G, Ng LL, Thompson M, Khan S, Samani NJ, Squire IB. Plasma matrix metalloproteinase-9 and left ventricular remodelling after acute myocardial infarction in man: a prospective cohort study. Eur Heart J. 2007;28:711-718. doi: 10.1093/eurheartj/ehm003.
20. Dhillon OS, Khan SQ, Narayan HK, Ng KH, Mohammed N, Quinn PA, Squire IB, Davies JE, Ng LL. Matrix metalloproteinase-2 predicts mortality in patients with acute coronary syndrome. Clin Sci (Lond) 2009;118:249-57. doi: 10.1042/CS20090226.
21. Kelly D, Khan S, Cockerill G, Ng LL, Thompson M, Samani NJ, Squire IB. Circulating stromelysin-1 (MMP-3): a novel predictor of LV dysfunction, remodelling and all-cause mortality after acute myocardial infarction. Eur J Heart Fail. 2008;10:133-139. doi: 10.1016/j.ejheart.2007.12.009.