



Novel Cardiac Biomarkers H-FABP and GPBB for Early Detection and Prognosis of Acute Myocardial Infarction

Hayder T Qaddoori ^{1*}, Fatima Mallalah Mohammed ², Ali Najm Abdullah ¹

Abstract

Background: Cardiovascular diseases are the leading cause of morbidity and mortality globally, with acute myocardial infarction (AMI) being a significant contributor. This study aimed to investigate the roles of cardiac biomarkers, including H-FABP, GPBB, and others, in detecting AMI. **Method:** Blood samples were collected from 80 individuals, including 50 with AMI and 30 healthy controls, admitted to the Coronary Care Unit (CCU) of an Educational Hospital in Diyala province between May and July 2022. Cardiac markers (hs-troponin-I, myoglobin, CK-MB, GPBB, and H-FABP) were measured using the Sandwich-ELISA technique. **Results:** There were no significant differences ($p>0.05$) in age or gender distribution between the study groups. Levels of cardiac markers were significantly higher in AMI patients compared to healthy controls ($p<0.05$). H-FABP demonstrated the highest sensitivity (100%), followed by GPBB (97%), hs-troponin-I (87%), CK-MB (85%), and myoglobin (78%), with significant differences ($p<0.05$) in detecting AMI. H-FABP and GPBB also exhibited the highest specificity (98% and 96%, respectively), while

myoglobin and CK-MB had lower specificity (82% and 84%, respectively). Furthermore, positive correlations were observed between H-FABP, GPBB, and other markers (hs-troponin-I, myoglobin, CK-MB). **Conclusion:** H-FABP and GPBB show promise as predictive indicators for early diagnosis (within 1-4 hours of chest pain) of AMI, offering potential utility in clinical practice.

Keywords: Acute myocardial infarction (AMI), H-FABP, GPBB, Cardiac Biomarkers.

Introduction

Cardiovascular diseases are the leading global cause of morbidity and mortality, resulting in an estimated 17.9 million deaths annually (Ibanez et al., 2018). Among these, acute myocardial infarction (AMI) and stroke account for over four-fifths of cardiovascular deaths, despite advances in treatment and prevention (Collet et al., 2021). AMI primarily stems from acute atherothrombotic blockage of coronary arteries, often compounded by plaque rupture or erosion (Ibanez et al., 2018). Recognition of acute myocardial injury, particularly through cardiac troponin (cTn) biomarkers, is pivotal in diagnosing myocardial infarction (Thygesen et al., 2019). Distinction between ST-elevation myocardial infarction (STEMI) and non-ST-elevation myocardial infarction (NSTEMI) guides intervention strategies, with STEMI typically associated with poorer short-term prognosis due to increased transmural ischemia (Ibanez et al., 2018). Early measurement of biomarker levels post-MI offers potential for precise risk stratification and tailored therapeutic interventions to

Significance | Novel cardiac biomarkers H-FABP and GPBB might improve the early diagnosis for myocardial infarction detection (within 1-4 hours of chest pain). H-FABP and GPBB proteins were investigated for identifying the heart muscle problems in this study.

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improve patient outcomes (Trinh et al., 2022).

Clinically ideal indicators for acute myocardial infarction (AMI) must exhibit cost-effectiveness, rapidity, precision, and high sensitivity and specificity. However, no single perfect indicator exists, posing a significant challenge for clinicians (Didangelos et al., 2009). Consequently, researchers have turned to proteomic techniques to identify novel prognostic indicators. Proteomic studies have revealed substantial alterations in the myocardial proteome following MI, shedding light on potential biomarkers. Moreover, proteomic analysis of unstable plaques has offered insights into the pathogenic mechanisms underlying plaque rupture (Stătescu et al., 2022).

The actin-myosin connection relies on structural proteins called troponins (T, I, and C) (cTnT, cTnI, and cTnC). These troponins are produced and released from cardiomyocytes in response to increased stretch or necrosis. Cardiac-specific troponins cTnT and cTnI serve as crucial predictive biomarkers for cardiac damage and acute myocardial infarction (AMI) (Berezin and Berezin, 2020). After an acute coronary syndrome (ACS), their levels typically rise within 2-4 hours, peak at 24 hours, and remain elevated for 2-3 weeks (Aydin et al., 2019).

Following a myocardial injury, creatine kinase-MB (CK-MB), an isoenzyme primarily found in cardiac cells and in small quantities in muscle tissue, is released into the bloodstream and typically returns to normal levels within 48-72 hours (Gho et al., 2017). Furthermore, Yang et al. demonstrated the significance of early CK-MB level monitoring in detecting left ventricular adverse remodeling post-acute myocardial infarction, which can lead to the development of heart failure (Yang et al., 2022).

A cytoplasmic protein known as heart-type fatty acid binding protein (H-FABP) plays a crucial role in myocardial lipid metabolism. Upon myocardial injury, its levels rapidly increase (within an hour), peak between four and six hours, and return to normal within 24 hours (Ye et al., 2018). As a result, it can serve as an early biomarker of acute myocardial infarction (AMI), potentially predicting reinfarction as it can be detected in plasma before cardiac troponin (cTn) (Moon et al., 2021). Studies have highlighted the association between H-FABP and stable coronary heart disease, serving as a separate predictor for cardiac disease and acute heart failure-related hospitalization, with higher H-FABP levels associated with a 1.5-fold greater risk of adverse outcomes (Zhang et al., 2020). Glycogen phosphorylase BB (GPBB), another emerging biomarker, rises within the first few hours following AMI onset, making it a potential early indicator of AMI before significant damage occurs (Singh et al., 2018). GPBB levels increase in most AMI patients within 1 to 4 hours of chest pain onset, peaking prior to CK-MB or troponin T, and returning to baseline within 1 to 2 days of AMI onset (Ghimire et al., 2022).

Myoglobin, a hemoprotein generated in the cytosol of striated muscle tissue, including the heart and skeletal muscles, has historically been used as an early diagnostic indicator for acute coronary syndrome (ACS) due to its rapid release into the bloodstream (within the first 30 minutes). However, interest has shifted towards troponins due to myoglobin's poor cardiac selectivity (Aydin et al., 2019; Mohammed et al., 2022). While research conducted two decades ago suggested that myoglobin could improve ACS diagnosis, recent data supporting this claim are lacking (Bodí et al., 2003). One study indicated a 6.9-fold increase in the risk of death with each unit increase in log-transformed myoglobin levels (Karaismailoğlu et al., 2018).

Acute myocardial infarction (AMI) primarily arises from acute atherothrombotic blockage of coronary arteries, with cardiac troponins (cTn) serving as crucial biomarkers for its detection. Distinctions between ST-elevation myocardial infarction (STEMI) and non-ST-elevation myocardial infarction (NSTEMI) determine intervention strategies, with STEMI associated with worse short-term outcomes. While no ideal biomarker exists, proteomic techniques offer promise in discovering prognostic indicators. Troponins, creatine kinase-MB (CK-MB), heart-type fatty acid binding protein (H-FABP), and glycogen phosphorylase BB (GPBB) are key biomarkers reflecting myocardial damage, with myoglobin, although rapidly released, lacking cardiac selectivity.

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The current study aimed to identify the functions of H-FABP, GPBB, and other cardiac indicators in patients with acute myocardial infarction.

Material and methods

Data Collection:

The study was conducted in Baquba, Diyala province, from May to July 2022. Blood samples were obtained from 50 acute myocardial infarction (AMI) patients (32 males, 18 females, aged 40-80 years) admitted to the Coronary Care Unit (CCU) of the Educational Hospital, following screening by a specialist doctor. Additionally, 30 blood samples were collected from healthy individuals (20 males,

10 females, aged 40-80 years) to serve as a control group. Both groups provided gender and age information.

ELISA:

Serum isolation was performed by centrifuging 5 mL of human blood at 3,000 rpm for 5 minutes. Cardiac indicators were detected using a multi-functional immune-assay analyzer (Opus, Dade Behring Diagnostics). The hs-troponin-I test utilized a sandwich enzyme-linked immunosorbent assay (ELISA) with specific polyclonal antibodies against the cardiac version of hs-troponin-I (Abbott Diagnostics, Illinois, USA). Myoglobin was quantified using a sandwich ELISA immunoassay with anti-myoglobin primary and secondary antibodies (Abcam, USA). CK-MB, GPBB, and H-FABP concentrations were measured using ELISA kits (Hycult Biotechnology, Uden, Netherlands).

Statistical Analysis:

Normality of cardiac marker concentrations was assessed using the Shapiro-Wilk and Kolmogorov-Smirnov tests, with all markers passing. Results were presented as Mean \pm SD, and means of numerical variables were compared using Student's t-test. The Pearson-Chi-square test determined differences in percentages of other characteristics. Pearson correlation coefficient (R) assessed the relationship strength between variables. Area under the curve (AUC), sensitivity, and specificity were calculated using unique receiver operating characteristic (ROC) curves for each parameter. Statistical analyses were performed using SPSS version 25.0 and GraphPad Prism version 6.

Results

Age Groups and Gender of Study Groups:

The research found no significant differences ($p>0.05$) in age and gender among the study groups. The age groups 51-60, 61-70, and >70 years had the highest percentages in patients (24.0%, 24.0%, and 40.0%, respectively) and healthy individuals (26.7%, 36.7%, and 23.3%, respectively), while the 41-50 years age group had the lowest percentage in patients (12.0%) compared to healthy individuals (13.3%). Males had higher percentages in both patients (66.7% and 64.0%) and healthy groups compared to females (Table 1).

Relation of Biochemical Parameters with Study Groups:

Significant differences ($P<0.05$) were observed between biochemical parameters and study groups. Patients exhibited higher levels of H-FABP, GPBB, Hs-Troponin I, myoglobin, and CKMB (32.58 \pm 7.56, 29.22 \pm 8.30, 31.38 \pm 6.20, 86.44 \pm 15.04, and 30.72 \pm 6.22, respectively) compared to healthy individuals (10.63 \pm 3.44, 11.37 \pm 5.79, 15.47 \pm 6.18, 68.20 \pm 19.89, and 19.60 \pm 9.43, respectively) (Table 2 and Figure 1).

Receiver Operator Characteristic (ROC) Curve of Parameters:

The study found high sensitivity for H-FABP (100%), followed by GPBB (97%), Hs-Troponin I (87%), CKMB (85%), and myoglobin (78%), with significant differences ($p<0.05$) in screening patients with myocardial infarction. H-FABP and GPBB exhibited the highest specificity (98% and 96%, respectively) compared to myoglobin and CKMB, which had lower specificity (82% and 84%, respectively) (Table 3 and Figure 2).

Correlation Study Among Biochemical Parameters:

A significant positive correlation was observed between H-FABP and GPBB (0.354*), Hs-Troponin I (0.529**), myoglobin (0.343*), and CKMB (0.313*). GPBB showed significant positive correlations with Hs-Troponin I (0.582**), myoglobin (0.303*), but no significant correlation with CKMB (0.033) (Table 4 and Figure 3).

Discussion

The present study aimed to investigate the relationship between age, gender, and biochemical parameters in patients with myocardial infarction (MI). The findings indicated no significant differences among age and gender in the study groups. However, biochemical parameters showed highly significant differences between patients and healthy individuals, with elevated levels of H-FABP, GPBB, Hs-Troponin I, Myoglobin, and CKMB observed in patients compared to healthy subjects.

Age and gender role

The age distribution among patients revealed that individuals aged 51-70 years accounted for the highest percentage of MI cases, with those over 70 years representing the largest proportion. This aligns with previous research by Beller et al. (2020), which found an increased incidence of MI in adults over 50. However, contradictory findings from Ambroziak et al. (2020) suggest a higher incidence of MI in young individuals. Ambroziak et al. (2020) attributed this to a family history of early MI/ischemic stroke, indicating the importance of assessing CVD risk in young adults with such familial backgrounds.

Regarding gender, the study found that males had a higher percentage of MI cases compared to females. This supports the findings of Miguel-Yanes et al. (2021), who reported a greater incidence of MI in men than in women. Conversely, Canto et al. (2012) found higher MI scores in women, contradicting the present study's results.

Further insights come from Smilowitz et al. (2017), who highlight a greater post-MI mortality risk among women with disruptive coronary artery disease (MI-CAD). Additionally, DeFilippis et al. emphasize that women who experience their first MI before the age of 50 are less likely to undergo recommended coronary revascularization or medical therapy, leading to increased cardiovascular and all-cause mortality compared to men.

Table 1. comparative age groups and gender with study groups were calculated by chi-square test.

			Groups		Total	Statistics
			Healthy (n=30)	Patients (n=50)		
Age groups (years)	41-50	n	4	6	10	P>0.05 1.11 (0.91-2.21)
		%	13.3%	12.0%	12.5%	
	51-60	n	8	12	20	P>0.05 1.21 (0.88-1.91)
		%	26.7%	24.0%	25.0%	
	61-70	n	11	20	31	P>0.05 0.91 (0.33-1.94)
		%	36.7%	40.0%	38.8%	
	>70	n	7	12	19	P>0.05 0.97 (0.45-1.88)
		%	23.3%	24.0%	23.8%	
Gender	Males	n	20	32	52	P>0.05 1.24 (0.87-2.19)
		%	66.7%	64.0%	65.0%	
	Females	n	10	18	28	P>0.05 0.92 (0.23-1.67)
		%	33.3%	36.0%	35.0%	

Table 2. comparative biochemical parameters with study groups were calculated by student t test

	Groups	N	Mean	SD	Statistics
H-FABP (ng/ml)	Patients	50	32.58	7.56	P<0.001****
	Healthy	30	10.63	3.44	
GPBB (ng/ml)	Patients	50	29.22	8.30	P<0.001****
	Healthy	30	11.37	5.79	
Hs-Troponin I (ng/l)	Patients	50	31.38	6.20	P<0.001****
	Healthy	30	15.47	6.18	
Myoglobin (ng/ml)	Patients	50	86.44	15.04	P<0.001****
	Healthy	30	68.20	19.89	
CKMB (IU/L)	Patients	50	30.72	6.22	P<0.001****
	Healthy	30	19.60	9.43	

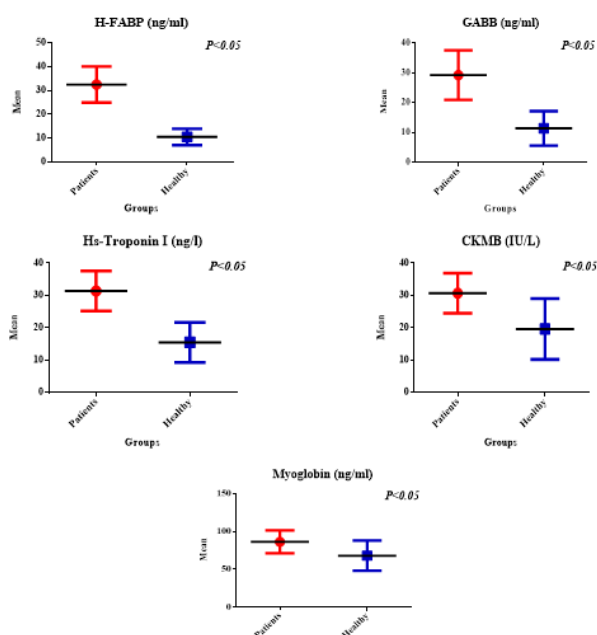


Figure 1. comparative biochemical parameters with study groups .

Table 3. ROC curve, sensitivity and specificity of biochemical parameters.

Variables	AUC	Std. Error	P value	Cut Off	Sensitivity %	Specificity %
H-FABP	1.000	.000	P<0.001****	≥15	100%	98%
GPBB	.952	.028	P<0.001****	>17	97%	96%
Hs-Troponin I	.883	.040	P<0.001****	≥14	87%	86%
Myoglobin	.761	.057	P<0.001****	>76	78%	82%
CKMB	.849	.057	P<0.001****	≥25	85%	84%

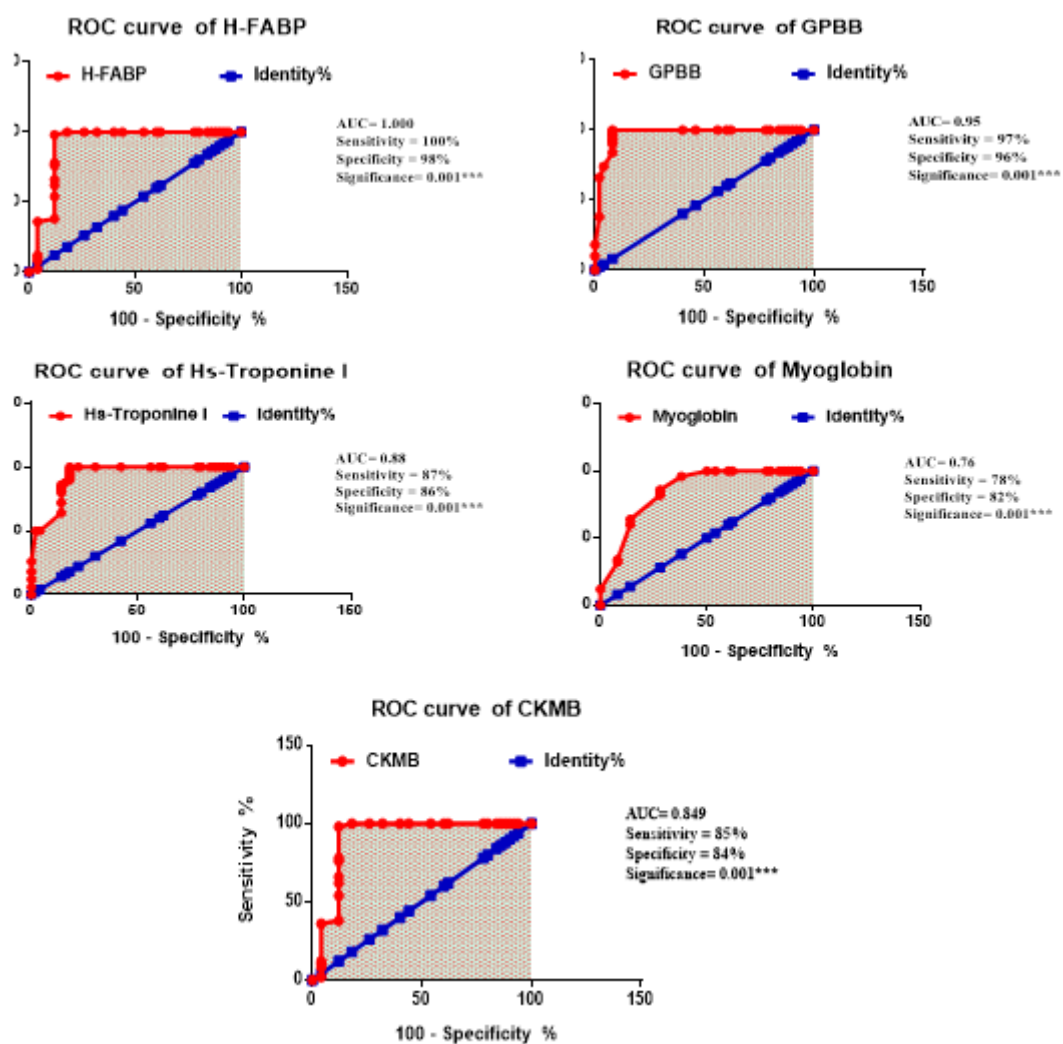


Figure 2. ROC curve of biochemical parameters

Table 4. Correlation relationship among biochemical parameters were calculated by pearson correlation

		H-FABP	GPBB
GPBB	Pearson coefficient	.354 [*]	1
	Significant	.012	
Hs-Troponin I	Pearson coefficient	.529 ^{**}	.582 ^{**}
	Significant	.000	.000
Myoglobin	Pearson coefficient	.343 [*]	.303 [*]
	Significant	.015	.033
CKMB	Pearson coefficient	.313 [*]	.173
	Significant	.027	.229

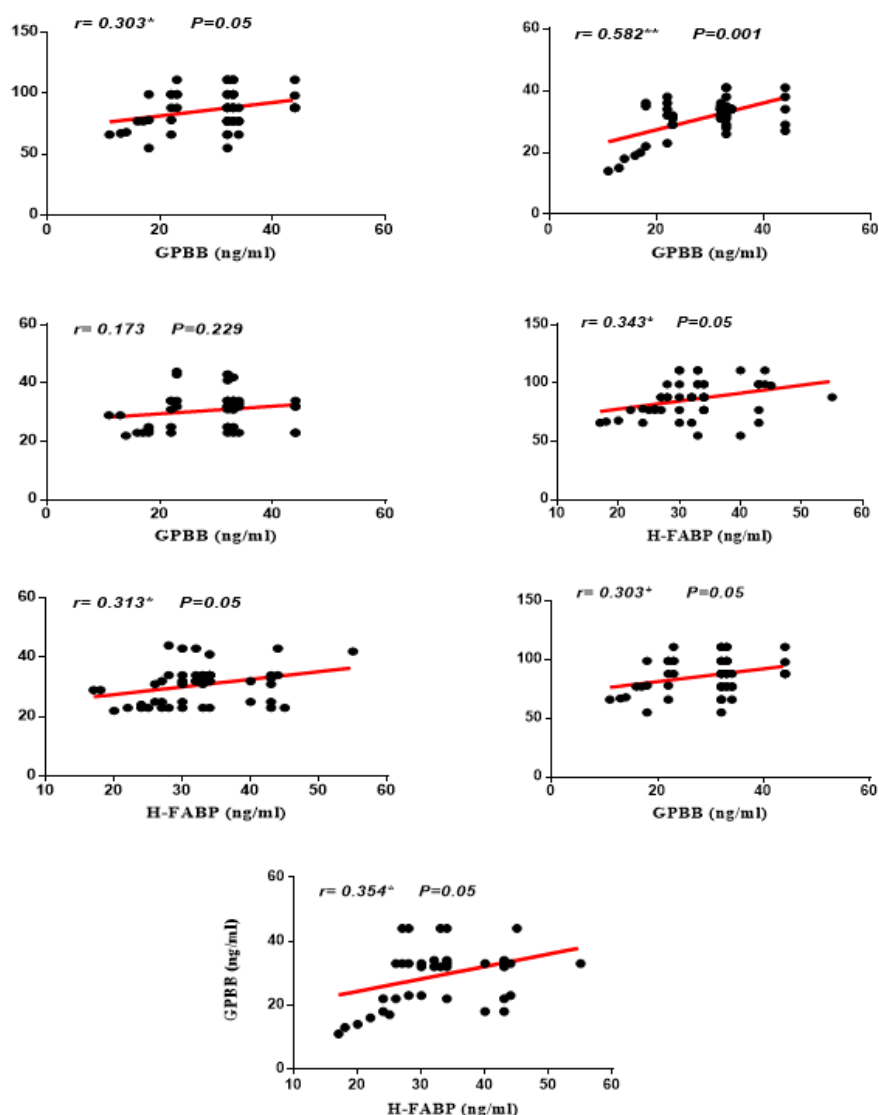


Figure 3. correlation relationship among biochemical parameters

COVID-19 role

The COVID-19 pandemic's impact on MI prevalence, particularly in women, has been noted by Huynh et al. (2021), indicating exacerbated sex inequalities in seeking medical attention for acute MI. Lorente-Ros et al. (2022) observed differences in therapeutic criteria for women with STEMI, leading to higher in-hospital death rates compared to men. Additionally, disparities in invasive procedures and in-hospital fatality rates were reported for women with STEMI (de Miguel-Yanes et al., 2021).

The COVID-19 pandemic has also influenced MI prevalence, as noted by Huynh et al. (2021), who observed a 15% decrease in acute MI worldwide during the pandemic. Remarkably, this decrease was more pronounced among women aged 70 or older, indicating exacerbated sex inequalities in seeking medical attention for acute MI in women compared to men (Redfors et al., 2015).

Women under the age of 55 experiencing ST-segment elevation myocardial infarction (STEMI) are subject to different therapeutic criteria compared to men, as indicated by Lorente-Ros et al. (2022). Despite the implementation of a network system for STEMI, Sambola et al. (2021) found that women are less likely to undergo primary percutaneous coronary intervention (pPCI) and have higher in-hospital death rates than men over an 11-year trial period. Furthermore, de Miguel-Yanes et al. (2021) discovered that women admitted for STEMI undergo invasive procedures less frequently and experience higher in-hospital fatality rates.

Biochemical markers role and potential mechanism

Biochemical markers play a crucial role in diagnosing and predicting MI. Elevated levels of H-FABP, GPBB, Hs-Troponin I, Myoglobin, and CKMB were observed in MI patients, consistent with previous research (Chaulin and Duplyakov, 2020). Troponins, particularly high-sensitivity assays, remain the gold standard for MI assessment (Wu et al., 2021), while H-FABP shows promise in early detection (Moon et al., 2021). GPBB has demonstrated diagnostic value, especially in the early hours post-symptom onset (Peetz et al., 2005). However, it may not enhance the diagnostic performance of high-sensitivity troponin I (Keller et al., 2011).

Biomarkers hold promise as effective tools for assessing the prognosis of myocardial infarction patients. Recent advancements in myocardial infarction marker research have been driven by increased understanding of additional mechanisms contributing to myocardial infarction pathophysiology, such as neurohormonal activation, myocardial stress, and inflammatory processes. However, further validation and investigation are necessary as there are currently no randomized trials examining the relationship between these biomarkers and their prognostic value in individuals with acute myocardial infarction (AMI). New biomarkers may offer opportunities for more personalized therapeutic approaches to improve patient outcomes (Stătescu et al., 2022).

CK-MB, although less specific, remains a useful marker for diagnosing AMI, especially in conjunction with troponins (Aydin et al., 2019). The CK-MB/Troponin ratio has shown diagnostic efficacy and prognostic value in assessing left ventricular activities post-STEMI (Eyyupkoca et al., 2021). Myoglobin, despite lacking specificity, is sensitive for early MI detection and exclusion (Asl and Rahimzadegan, 2022).

A suitable biomarker for acute myocardial infarction (AMI) should exhibit accuracy, sensitivity, and strong prognostic accuracy in the early stages of disease progression to assist doctors in selecting optimal treatment strategies. However, there is currently no perfect biomarker for AMI that possesses all these qualities simultaneously. The most reliable indicators for diagnosing and predicting AMI are currently recognized as cardiac troponin T (cTnT) and cardiac troponin I (cTnI), which can be detected using highly and moderately sensitive techniques, respectively. Despite their utility, highly sensitive indicators such as CP-K-MB, GPBB, myoglobin, and hFABP have limited specificity in AMI diagnosis and therefore cannot serve as primary biomarkers (Chaulin and Duplyakov, 2020).

The current investigation revealed that patients had greater levels of H-FABP, GPBB, Hs-Troponin I, Myoglobin, and CKMB markers than healthy individuals did. These findings were in line with those of Chaulin and Duplyakov (2020). MI is a systemic aging illness influenced by a variety of genetic, ecological, and lifestyle variables. The heart muscle produces and releases cardiac peptides. The primary structure of the striated cardiac muscle is created by interactions between these peptides and tropomyosin. Cardiac troponin (cTn) controls the calcium-dependent association between actin and myosin, which in turn affects myocardial contraction. There are numerous tissue-specific cTn isoforms (Anderson et al., 1991). Despite the large amount of cTn in the contractile apparatus, the quantity of TnC in the cytosolic pool is comparable to the quantity of CK-MB. Thus, the concentration of TnC per gram of myocardium is 13–15 times greater than that of CK-MB. The increased level of cTn in peripheral blood notwithstanding the normal level of CK-MB following cardiac tissue injury of less than 1 g (due to ischemia, infarction, trauma, toxic damages, or inflammation) can therefore be explained by the earlier period's improved sensitivity of cTn compared with CK-MB. It is a crucial biochemical indicator for the identification of AMI, according to the American College of Cardiology (ACC) and European Society of Cardiology (ESC), for these reasons. Cardiac troponins are noticeably raised in a variety of clinical situations, but coronary ischemia is the disease for which they have the highest sensitivity and specificity. There really are medical situations other than acute myocardial infarction (AMI) in which troponins may be elevated. TnC levels in serum are typically modest in healthy individuals, but they rise in cases of myocyte injury because of

releases from the cytosolic pool in the early stages and the contractile apparatus in the late stages into the peripheral blood. As a result, following acute myocardial injury, blood levels rise between 2–four hours and maximum around 24 hours. For 1–2 weeks, blood cTn levels are elevated. Contrary to the CK-MB level, the late period's continued release of cTn from the contractile apparatus is what causes the long-lasting rise. Given that high-sensitivity cardiac troponin (hs-cTn) is the particular marker for heart tissue injury, it makes sense that it is the current gold-standard for AMI assessment. However, additional circulation indicators are required for assessing treatment outcomes, prediction, and prophylaxis. A recent study found that Hs-troponin I was crucial for the early detection and treatment of AMI (Karpay et al., 2022).

In contrast to the well-described kinetic profile of troponins in normotherm AMI patients, concentrations of both hs-cTnI and hs-cTnT stayed increased for 72 h in comatose out-of-hospital cardiac arrest (OHCA) survivors with an aetiology of AMI. The kinetic profiles of the two high sensitivity tests were identical. The kinetics of the troponins were unaffected by different targeted temperature management (TTM) durations, according to Larsen et al. (2022).

Newer than cTn, the heart-type fatty acid-binding protein (H-FABP) is a biomarker of myocardial damage. This could possibly play a significant role in both the earlier detection of high-risk patients who present shortly after the onset of CP as well as the quick risk-stratification of low-risk patients because it is abundantly present in the myocellular cytoplasm and therefore is released quickly (within 1 hour) after the onset of myocardial injury. Similar to cTn, H-FABP may also serve as a prognostic indicator in other disorders that result in myocardial damage, such as acute pulmonary embolism (PE) and acute congestive heart failure (CHF) (Goel et al., 2020).

Given the various circulatory discharge timings of cardiac markers after myocardial injury, researchers postulated that H-FABP would be helpful in the early identification of AMI (McCann et al., 2008). The AUC values measured the accuracy of H-FABP and TnI in the identification of AMI using lab tests and showed no statistically significant difference. Nevertheless, H-FABP revealed the best diagnostic value in patients presenting between 4 and 24 hours following the onset of symptoms, while TnI indicated the greatest prognostic value in those appearing between 4 and 8 hours, with no statistical evidence found (Moon et al., 2021).

H-FABP may be beneficial in the early identification of AMI, according to certain research, despite the lack of general agreement over its diagnostic value. Within 2 to 3 hours of myocardial damage, H-FABP was first identified in the prior study, preceded by TnI and CK-MB. Interestingly, relative to other peptides, H-FABP is easily released into circulatory system since it is a tiny soluble protein. Early diagnosis is also facilitated by its low threshold (Moon et al., 2021).

An algorithm using heart fatty acid binding protein (h-FABP), high-sensitivity troponin (hs-cTn), and electrocardiogram (ECG) shows good precision and therefore can screen out up to 40% of individuals who report to the emergency room with breathing difficulties. An approach that solely uses the electrocardiogram (ECG) and hs-cTn has a similar sensitivity and may exclude a greater percentage of patients. When a patient presents to the emergency room, any of the methods can be employed to appropriately designate them as being at low risk for AMI (Van Hise et al., 2018).

GPBB (glycogen phosphorylase BB) is widely distributed in healthy brain and myocardial tissues. The essential enzyme for glycogenolysis is GPBB, which is attached to the cardiomyocytes' sarcoplasmic reticulum glycogenolytic complex (Entman et al., 1977). The degree of connection between GP and the sarcoplasmic reticulum glycogenolytic complex is determined by the myocardial metabolic state, which is discovered to be extremely sensitive to ischemia-induced glycogenolysis. The confined form of GPBB transforms into a soluble cytosolic form after ischemia and phosphorolysis. Similar to cardiac ischemia, enhanced glycogenolysis and loss of cell membrane integrity cause GPBB to be released into the extracellular environment via the T-tubule system (Rabitzsch et al., 1995). It is more plausible that the rise in plasma GPBB level during breathing difficulties is primarily due to the GPBB discharge from the heart because the blood-brain barriers typically stays unchanged in MI patients.

Recent investigations revealed that several of the other indicators, such as myoglobin and CK-MB, have lower sensitivity and specificity in the early hours (within 4 hours of discomfort onset) (Singh et al., 2018). Early clinical studies revealed that GPBB tests have higher sensitivity and better specificity than other indicators, such as the first-generation cardiac troponin T, for the early diagnosis of myocardial infarction (Peetz et al., 2005). Surprisingly, current research indicates that high GPBB may provide predictive data further than that provided by hscTnI and brain natriuretic peptide (BNP). Additionally, it has been identified a link between an incredibly high level of GPBB in a patient with clinical signs of ACS and a worse midterm prognosis (Lillpopp et al., 2012). A research for the identification of anthracycline-induced cardiotoxicity and carbon monoxide-associated cardiotoxicity, which are both related to ischemic pathophysiology, indicated that GPBB was superior than cTnI and cTnT. (El-Nagdy et al., 2020).

It's been demonstrated that using cardiac troponin and heart-type fatty acid-binding protein (H-FABP) at the point of admission improves diagnostic outcomes, particularly in the early hours after presenting. Additionally, recent research has shown that GPBB doesn't really enhance the diagnostic performance of high-sensitivity troponin I in patients with suspected acute coronary syndrome (Keller et al., 2011). No single indicator, includes GPBB,

is superior to high-sensitive cardiac troponins for the diagnosis of acute myocardial infarction, according to a recent survey examining several indicators for MI (Ghimire et al., 2022).

The cardiac, muscle fibers, small bowel, diaphragm, uterus, tongues, and prostate all contain creatine kinase-MB (CK-MB). AMI can be diagnosed with sensitivity and specificity thanks to the MB form of CK, which makes up around 20% of all CK in the myocardium. Muscular system makes up 5% of its composition. As a result, its specificity is diminished by its rising level after trauma and inflammation. Because of its high molecular mass, another drawback of CK-MB is that it does not identify small myocardial injury. Within 24 hours, CK-MB reaches its peak. It then begins to rise 4–9 hours after myocardial damage and declines to the range of normal 48–72 hours later. Infarct size is associated with total CK and CK-MB values, which are significant prognostic indicators. Additionally, it has also been discovered that CK-MB activity is more accurate and precise than CK-MB mass assessments (Aydin et al., 2019).

Additionally helpful in assessing reperfusion is CK-MB. It starts to rise after 1–2 g of myocardial injury. At least 10 to 12 hours after the onset of symptoms should have passed for the identification of AMI to be conclusive. Within 10–12 hours after the onset of symptoms, it has a 97% specificity. If sequential follow-up includes 24–48 hours, this sensitivity is quite excellent. During 4–6 hours of the discomfort, if the ECG result doesn't corroborate the CK-MB value, it loses significance (Aydin et al., 2019).

The level of Troponin and CK-MB altered in the prior study in a manner that was consistent with the results of other studies. Within the initial hours of the patient's hospitalization, the serum concentrations of troponin rose steadily until they peaked and remained high for the following two to three weeks. Although CK-MB showed the same upward trend as Troponin, it has since reduced and will return to normal during the next 48–72 hours. Several studies showed that CK-MB is no longer considered to be an emergency indicator and can be used to determine the extent of infarcts and their prognosis (Shahbazi et al., 2021).

Previous research demonstrated that, regardless of the conventional risk factors, the cTnT/CK-MB ratio >3.1 showed a greater sensitivity and negative predictive value when opposed to its components in detecting alterations in the left ventricular (LV) activities following ST-segment elevation AMI (STEMI). The cTnT/CK-MB ratio may perform diagnostically more effectively than cTnT and CK-MB by themselves. In clinical practice, the cTnT/CK-MB ratio can be utilized for risk classification and therapy optimization (Eyyupkoca et al., 2021).

With a molecular weight of 16.8 kDa, myoglobin is a protein that binds iron and oxygen and is widely distributed in muscle tissue and the hearts of mammals. Although myoglobin is only contained in muscle fibers, muscular injury can cause it to enter the bloodstream.

It has no specificity; however, it is a sensitive sign for AMI. Within 24 hours of the lesion, it is quickly liberated from the myocardium and quickly eliminated from the kidneys (Klocke et al., 1982). Because of its rapid kinetics, myoglobin rises within the first thirty minutes of the early phase following the commencement of an acute episode, making it a crucial indicator for the early diagnosis and/or exclusion of cardiac injury (Asl and Rahimzadegan, 2022). Across all AMI patients, it rises within 6 to 10 hours and reaches its peak at 12 hours. Positive numbers are less significant in the clinic because it lacks specificity than negative values (Aydin et al., 2019).

Summary of findings

This study demonstrated for the first time a substantial correlation between serum myoglobin and LGE on CMR in acute myocarditis and suggested that myoglobin may be used as a proxy for serious myocardial injury in myocarditis individuals. Myoglobin testing is a common laboratory procedure in emergency rooms; hence it may be useful in assisting in CMR triage. In institutions lacking a CMR infrastructure when individuals are moved to a tertiary care facility for further scanning, this could be especially useful (Kottwitz et al., 2020; Gavali et al., 2024).

Therefore, age and gender are important factors in MI incidence, with older individuals and males showing higher prevalence. Biochemical markers, particularly troponins, H-FABP, GPBB, CK-MB, and Myoglobin, play crucial roles in MI diagnosis and prognosis. Further research is warranted to validate the diagnostic and prognostic value of these biomarkers and to explore personalized treatment approaches for MI patients. The integration of these findings into clinical practice could improve MI management and outcomes.

Conclusion

In conclusion, the comparison of cardiac biomarkers such as heart-type fatty acid-binding protein (H-FABP) and glycogen phosphorylase BB (GPBB) with others like Hs-Troponin, myoglobin, and CKMB reveals their superior sensitivity and specificity, particularly for the early detection of myocardial infarction within 1–4 hours of chest pain onset. These findings suggest that GPBB and H-FABP could serve as valuable predictors for acute myocardial infarction, facilitating rapid diagnosis and timely intervention.

This study addressed the challenge of secretive and unrecognized myocardial infarction, which might contribute significantly to cardiovascular morbidity and mortality worldwide. By investigating the role of H-FABP and GPBB proteins as markers for identifying patients with heart muscle issues, this research contributes to enhancing early diagnosis capabilities. The use of these markers demonstrates the potential to diagnose acute myocardial infarction promptly, particularly within the critical early hours following symptom onset.

Given the staggering global burden of cardiovascular diseases and the need for more precise diagnostic tools, novel cardiac biomarkers like H-FABP and GPBB offer promising prospects for improving diagnostic accuracy and timely intervention in cases of myocardial infarction. By leveraging these markers, healthcare professionals can enhance their ability to identify and manage cardiovascular conditions effectively, ultimately reducing morbidity and mortality associated with these diseases.

Author contribution

H.T.Q. conceptualized and supervised, F.M.M. analyzed data, A.N.A. provided resources. All authors wrote the original draft, and reviewed, edited, and finalized the manuscript.

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Competing financial interests

The authors have no conflict of interest.

References

- Ambroziak, M., Niewczas-Wieprzowska, K., Maicka, A., & Budaj, A. (2020). Younger age of patients with myocardial infarction is associated with a higher number of relatives with a history of premature atherosclerosis. *BMC Cardiovascular Disorders*, 20, 1-9.
- Anderson, P. A., Malouf, N. N., Oakeley, A. E., Pagani, E. D., & Allen, P. D. (1991). Troponin T isoform expression in humans. A comparison among normal and failing adult heart, fetal heart, and adult and fetal skeletal muscle. *Circulation research*, 69(5), 1226-1233.
- Asl, S. K., & Rahimzadegan, M. (2022). The recent progress in the early diagnosis of acute myocardial infarction based on myoglobin biomarker: Nano-aptasensors approaches. *Journal of Pharmaceutical and Biomedical Analysis*, 211, 114624.
- Aydin, S., Ugur, K., Aydin, S., Sahin, İ., & Yardim, M. (2019). Biomarkers in acute myocardial infarction: current perspectives. *Vascular health and risk management*, 1-10.
- Beller, J., Bauersachs, J., Schäfer, A., Schwettmann, L., Heier, M., Peters, A., ... & Geyer, S. (2020). Diverging trends in age at first myocardial infarction: evidence from two German population-based studies. *Scientific reports*, 10(1), 9610.
- Berezin, A. E., & Berezin, A. A. (2020). Adverse cardiac remodelling after acute myocardial infarction: old and new biomarkers. *Disease Markers*, 2020.
- Bodí, V., Sanchis, J., Llácer, À., Fàcila, L., Núñez, J., Pellicer, M., ... & Chorro, F. J. (2003). Prognostic markers of non-ST elevation acute coronary syndromes. *Revista española de cardiología*, 56(9), 857-864.
- Bodor, G. S. (2016). Biochemical markers of myocardial damage. *Ejifcc*, 27(2), 95.
- Canto, J. G., Rogers, W. J., Goldberg, R. J., Peterson, E. D., Wenger, N. K., Vaccarino, V., ... & NRM Investigators. (2012). Association of age and sex with myocardial infarction symptom presentation and in-hospital mortality. *Jama*, 307(8), 813-822.
- Chaulin, A. M., & Duplyakov, D. V. (2020). Biomarkers of acute myocardial infarction: diagnostic and prognostic value. Part 1. *Journal of Clinical Practice*, 11(3), 75-84.
- Collet, J. P., Thiele, H., Barbato, E., Barthélémy, O., Bauersachs, J., Bhatt, D. L., ... & Siontis, G. C. (2021). ESC Scientific Document Group. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. *Eur Heart J*, 42(14), 1289-1367.
- de Miguel-Yanes, J. M., Jiménez-García, R., Hernandez-Barrera, V., de Miguel-Díez, J., Muñoz-Rivas, N., Méndez-Bailón, M., ... & Lopez-de-Andres, A. (2021). Sex differences in the incidence and outcomes of acute myocardial infarction in Spain, 2016–2018: a matched-pair analysis. *Journal of Clinical Medicine*, 10(8), 1795.
- DeFilippis, E. M., Collins, B. L., Singh, A., Biery, D. W., Fatima, A., Qamar, A., ... & Blankstein, R. (2020). Women who experience a myocardial infarction at a young age have worse outcomes compared with men: the Mass General Brigham YOUNG-MI registry. *European heart journal*, 41(42), 4127-4137.
- Didangelos, A., Simper, D., Monaco, C., & Mayr, M. (2009). Proteomics of acute coronary syndromes. *Current atherosclerosis reports*, 11(3), 188-195.
- El-Nagdy, S. A., Elfakharany, Y., & Etewa, R. (2020). Role of glycogen phosphorylase in prediction of cardiotoxicity associated with acute carbon monoxide poisoning. *Zagazig Journal of Forensic Medicine*, 18(2), 59-74.
- Entman, M. L., Bornet, E. P., Van Winkle, W. B., Goldstein, M. A., & Schwartz, A. (1977). Association of glycogenolysis with cardiac sarcoplasmic reticulum: II. effect of glycogen depletion, deoxycholate solubilization and cardiac ischemia: evidence for a phosphorylase kinase membrane complex. *Journal of Molecular and Cellular Cardiology*, 9(7), 515-528.
- Eyyupkoca, F., Felekoglu, M. A., Karakus, G., Kocak, A., Yildirim, O., Altintas, M. S., ... & Ozkan, C. (2021). The evaluation of cTnT/CK-MB ratio is as a predictor of change in cardiac function after myocardial infarction. *Heart, Vessels and Transplantation*, 5(3), 113-122.
- Gavali, L. V., Mohammed, A. A., Al-Ogaili, M. J., Gaikwad, S. H., Kulkarni, M., Das, R., & Ubale, P. A. (2024). Novel terephthalaldehyde bis (thiosemicarbazone) Schiff base ligand and its transition metal complexes as antibacterial Agents: Synthesis, characterization and biological investigations. *Results in Chemistry*, 7, 101316.
- Ghimire, A., Giri, S., Khanal, N., Rayamajhi, S., Thapa, A., Bist, A., & Devkota, S. (2022). Diagnostic accuracy of glycogen phosphorylase BB for myocardial infarction: A systematic review and meta-analysis. *Journal of Clinical Laboratory Analysis*, 36(5), e24368.
- Gho, J. M., Postema, P. G., Conijn, M., Bruinsma, N., de Jong, J. S., Bezzina, C. R., ... & Asselbergs, F. W. (2017). Heart failure following STEMI: a contemporary cohort study of incidence and prognostic factors. *Open Heart*, 4(2), e000551.
- Goel, H., Melot, J., Krinock, M. D., Kumar, A., Nadar, S. K., & Lip, G. Y. (2020). Heart-type fatty acid-binding protein: an overlooked cardiac biomarker. *Annals of Medicine*, 52(8), 444-461.

- Huynh, J., Barmano, N., Karlsson, J. E., & Stomby, A. (2021). Sex and age differences in the incidence of acute myocardial infarction during the COVID-19 pandemic in a Swedish health-care region without lockdown: a retrospective cohort study. *The Lancet Healthy Longevity*, 2(5), e283-e289.
- Ibanez, B., James, S., Agewall, S., Antunes, M. J., Bucciarelli-Ducci, C., Bueno, H., ... & Widimský, P. (2018). 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *European heart journal*, 39(2), 119-177.
- Karaismalloğlu, E., Dikmen, Z. G., Akbiyik, F., & Karaağaoğlu, A. E. (2018). A statistical approach to evaluate the performance of cardiac biomarkers in predicting death due to acute myocardial infarction: time-dependent ROC curve. *Turkish journal of medical sciences*, 48(2), 237-245.
- Karpay, S., Sarada, C. V., Kondu, D., Pavuluri, P., Gadepalli, R., & Naresh, B. (2022). Evaluation of biochemical parameters in acute myocardial infarction and angina patients. *Journal of Ideas in Health*, 5(2), 664-668.
- Keller, T., Zeller, T., Ojeda, F., Tzikas, S., Lillpop, L., Sinning, C., ... & Blankenberg, S. (2011). Serial changes in highly sensitive troponin I assay and early diagnosis of myocardial infarction. *Jama*, 306(24), 2684-2693.
- Klocke, F. J., Copley, D. P., Krawczyk, J. A., & Reichlin, M. (1982). Rapid renal clearance of immunoreactive canine plasma myoglobin. *Circulation*, 65(7), 1522-1528.
- Kottwitz, J., Bruno, K. A., Berg, J., Salomon, G. R., Fairweather, D., Elhassan, M., ... & Heidecker, B. (2020). Myoglobin for detection of high-risk patients with acute myocarditis. *Journal of cardiovascular translational research*, 13, 853-863.
- Larsen, A. I., Grejs, A. M., Vistisen, S. T., Strand, K., Skadberg, Ø., Jeppesen, A. N., ... & Søreide, E. (2022). Kinetics of 2 different high-sensitive troponins during targeted temperature management in out-of-hospital cardiac arrest patients with acute myocardial infarction: a post hoc sub-study of a randomised clinical trial. *BMC Cardiovascular Disorders*, 22(1), 342.
- Lillpop, L., Tzikas, S., Ojeda, F., Zeller, T., Baldus, S., Bickel, C., ... & Keller, T. (2012). Prognostic information of glycogen phosphorylase isoenzyme BB in patients with suspected acute coronary syndrome. *The American journal of cardiology*, 110(9), 1225-1230.
- Lorente-Ros, M., Patel, A., Lorente, J. A., & López-de-Sá, E. (2022). Sex related differences in the treatment of ST-segment elevation acute myocardial infarction in patients aged < 55 years. *The American Journal of Cardiology*, 170, 25-30.
- McCann, C. J., Glover, B. M., Menown, I. B., Moore, M. J., McEneny, J., Owens, C. G., ... & Adgey, J. A. (2008). Novel biomarkers in early diagnosis of acute myocardial infarction compared with cardiac troponin T. *European heart journal*, 29(23), 2843-2850.
- Mohammed, Z. J., Sharba, M. M., & Mohammed, A. A. (2022). The effect of cigarette smoking on haematological parameters in healthy college students in the capital, baghdad. *European Journal of Molecular & Clinical Medicine*.
- Moon, M. G., Yoon, C. H., Lee, K., Kang, S. H., Youn, T. J., & Chae, I. H. (2021). Evaluation of heart-type fatty acid-binding protein in early diagnosis of acute myocardial infarction. *Journal of Korean Medical Science*, 36(8).
- Peez, D., Post, F., Schinzel, H., Schweigert, R., Schollmayer, C., Steinbach, K., ... & Lackner, K. J. (2005). Glycogen phosphorylase BB in acute coronary syndromes. *Clinical Chemistry and Laboratory Medicine (CCLM)*, 43(12), 1351-1358.
- Rabitzsch, G., Mair, J., Lechleitner, P., Noll, F., Hofmann, U., Krause, E. G., ... & Puschendorf, B. (1995). Immunoenzymometric assay of human glycogen phosphorylase isoenzyme BB in diagnosis of ischemic myocardial injury. *Clinical chemistry*, 41(7), 966-978.
- Redfors, B., AngerAas, O., RAamunddal, T., Petursson, P., Haraldsson, I., Dworeck, C., ... & Omerovic, E. (2015). Trends in gender differences in cardiac care and outcome after acute myocardial infarction in Western Sweden: a report from the Swedish web system for enhancement of evidence-based care in heart disease evaluated according to recommended therapies (SWEDEHEART). *Journal of the American Heart Association*, 4(7), e001995.
- Sambola, A., Elola, F. J., Ferreiro, J. L., Murga, N., Rodríguez-Padial, L., Fernández, C., ... & Anguita, M. (2021). Impact of sex differences and network systems on the in-hospital mortality of patients with ST-segment elevation acute myocardial infarction. *Revista Española de Cardiología (English Edition)*, 74(11), 927-934.
- Shahbazi, H., Maleknia, M., & Noroozi, S. (2021). Investigating the Association of IL-1beta IL-8 & IL 11 with Commonly used Cardiovascular Biomarkers (CK-MB & Troponin) in Patients with Myocardial Infarction (MI).
- Singh, N., Rathore, V., Mahat, R. K., & Rastogi, P. (2018). Glycogen phosphorylase BB: a more sensitive and specific marker than other cardiac markers for early diagnosis of acute myocardial infarction. *Indian Journal of Clinical Biochemistry*, 33(3), 356-360.
- Smilowitz, N. R., Mahajan, A. M., Roe, M. T., Hellkamp, A. S., Chiswell, K., Gulati, M., & Reynolds, H. R. (2017). Mortality of myocardial infarction by sex, age, and obstructive coronary artery disease status in the ACTION Registry—GWTG (Acute Coronary Treatment and Intervention Outcomes Network Registry—Get With the Guidelines). *Circulation: Cardiovascular Quality and Outcomes*, 10(12), e003443.
- Stătescu, C., Anghel, L., Tudurachi, B. S., Leonte, A., Benchea, L. C., & Sascău, R. A. (2022). From classic to modern prognostic biomarkers in patients with acute myocardial infarction. *International Journal of Molecular Sciences*, 23(16), 9168.
- Thygesen, K., Alpert, J. S., Jaffe, A. S., Chaitman, B. R., Bax, J. J., Morrow, D. A., & White, H. D. (2019). Fourth universal definition of myocardial infarction (2018). *European heart journal*, 40(3), 237-269.
- Trinh, K., Julovi, S. M., & Rogers, N. M. (2022). The role of matrix proteins in cardiac pathology. *International Journal of Molecular Sciences*, 23(3), 1338.
- Van Hise, C. B., Greenslade, J. H., Parsonage, W., Than, M., Young, J., & Cullen, L. (2018). External validation of heart-type fatty acid binding protein, high-sensitivity cardiac troponin, and electrocardiography as rule-out for acute myocardial infarction. *Clinical biochemistry*, 52, 161-163.

- Wessler, J. D., Stant, J., Duru, S., Rabbani, L., & Kirtane, A. J. (2015). Updates to the ACCF/AHA and ESC STEMI and NSTEMI guidelines: putting guidelines into clinical practice. *American Journal of Cardiology*, 115(5), 23A-28A.
- Wu, Y., Pan, N., An, Y., Xu, M., Tan, L., & Zhang, L. (2021). Diagnostic and prognostic biomarkers for myocardial infarction. *Frontiers in cardiovascular medicine*, 7, 617277.
- Yang, Y., Liu, J., Zhao, F., Yuan, Z., Wang, C., Chen, K., & Xiao, W. (2022). Analysis of correlation between heart failure in the early stage of acute myocardial infarction and serum pregnancy associated plasma protein-A, prealbumin, C-reactive protein, and brain natriuretic peptide levels. *Annals of Palliative Medicine*, 11(1), 264-234.
- Ye, X. D., He, Y., Wang, S., Wong, G. T., Irwin, M. G., & Xia, Z. (2018). Heart-type fatty acid binding protein (H-FABP) as a biomarker for acute myocardial injury and long-term post-ischemic prognosis. *Acta pharmacologica sinica*, 39(7), 1155-1163.
- Zhang, H. W., Jin, J. L., Cao, Y. X., Liu, H. H., Zhang, Y., Guo, Y. L., ... & Li, J. J. (2020). Heart-type fatty acid binding protein predicts cardiovascular events in patients with stable coronary artery disease: a prospective cohort study. *Annals of Translational Medicine*, 8(21).