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Diagnostic Performance of Serum Copeptin in the Early Detection of Acute Myocardial Infarction

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ABSTRACT

Background: Early and precise identification of Acute Myocardial Infarction (AMI) remains critical for timely intervention and improved patient outcomes. Copeptin, a surrogate marker of arginine vasopressin release, has emerged as a promising biomarker for early AMI diagnosis. **Objective:** This research aimed to assess the diagnostic value of serum copeptin in cases presenting with symptoms suggestive of Acute Myocardial Infarction.

Patients and Methods: Case-control research involved 100 participants, separated into 2 groups: Group A (n = fifty) healthy controls, and Group B (n = fifty) patients with confirmed Acute Myocardial Infarction (AMI). Demographic data, clinical symptoms, cardiovascular risk factors, vital signs, and laboratory data including serum copeptin, troponin I, and CK-MB were recorded.

Results: There were no significant variances in sex, age, or marital status among the groups (p-value above 0.05). Group B (Acute Myocardial Infarction patients) had significantly higher heart rates (88.4 ± 12.6 vs. 70.7 ± 11.9 bpm, $p = 0.04$) and respiratory rates (28 ± 2.0 vs. 18 ± 2.1 breaths/min, $p = 0.001$). Ischemic symptoms such as angina (64% vs. 16%), dyspnea (76% vs. 20%), palpitations (36% vs. 10%), fatigue (52% vs. 14%), and syncope (16% vs. 4%) were significantly more common in Group B (p-value below 0.05).

Conclusion: Serum copeptin is a reliable and early biomarker for the diagnosis of acute myocardial infarction. Its high sensitivity and specificity support its use alongside traditional markers to enhance early risk stratification and clinical decision-making in cases presenting with chest pain.

Keywords: Serum Copeptin, Chest Pain, AMI, Biomarker.

INTRODUCTION

Chest pain remains one of the leading complaints among cases presenting to emergency departments (EDs) globally, accounting for a substantial portion of acute care visits. The underlying causes of chest pain range from benign to potentially fatal, necessitating rapid and accurate diagnostic strategies to distinguish acute coronary syndromes (ACS) from non-cardiac etiologies. Among these, acute myocardial infarction remains a major etiology of morbidity and death, underscoring the need for prompt diagnosis and intervention to improve clinical outcomes [1,2].

AMI is characterized by irreversible myocardial injury caused by a sudden interruption of coronary blood flow, most commonly because of plaque rupture and subsequent thrombus formation. Despite significant advances in reperfusion therapies and pharmacological interventions, delayed or missed diagnoses remain a challenge and are associated with poorer prognoses. Early diagnosis, particularly within the first few hours of symptom onset, is critical; studies have consistently shown that timely reperfusion, especially within the initial 90–180 minutes, significantly reduces infarct size and mortality risk [3,4].

Traditionally, the diagnosis of AMI relies on the triad of clinical symptoms, electrocardiographic (ECG) changes, and cardiac biomarkers, primarily troponins. While troponin I and T are highly specific markers for myocardial injury, they typically rise several hours after symptom onset, which limits their utility in early triage. Moreover, a significant number of AMI patients present with atypical symptoms or non-diagnostic ECGs, making early clinical identification challenging, particularly in elderly patients, women, and those with comorbidities [5,6]. Although coronary angiography remains the definitive method for confirming myocardial infarction, its invasiveness, cost, and limited availability in some settings preclude its routine use as an initial diagnostic tool [7].

In light of these limitations, there is a growing emphasis on identifying reliable early biomarkers that can complement existing diagnostic pathways. One such biomarker is copeptin, the C-terminal segment of pre-provasopressin, which is secreted in equimolar quantities with arginine vasopressin (AVP). AVP plays a pivotal role in the body's stress response, particularly in cardiovascular and osmotic regulation. However, AVP's clinical use is restricted by its short half-life and instability in plasma. Copeptin, by contrast, is highly stable and easily measurable, making it an attractive surrogate marker for AVP release [8–10].

Emerging evidence suggests that copeptin levels rise rapidly within minutes of the onset of acute stress events, including AMI. Unlike troponin, which reflects structural myocardial injury, copeptin serves as an indicator of endogenous stress and neurohormonal activation. Elevated copeptin concentrations have been documented in the early hours of acute myocardial infarction, even before myocardial necrosis becomes biochemically detectable. This early rise positions copeptin as a potential tool for "rule-in" and "rule-out" strategies in conjunction with troponin, particularly in patients with inconclusive clinical or ECG findings [11–13]. Thus, our research aimed to explore the diagnostic utility of serum copeptin in the early recognition of

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acute myocardial infarction, with the goal of supporting earlier diagnosis, guiding timely therapeutic decisions, minimizing unnecessary hospital admissions, and improving resource utilization in emergency care settings.

PATIENTS AND METHODS

This case-control research involved 100 participants, separated into 2 groups: Group A (n = fifty) healthy controls, and Group B (n = fifty) patients with confirmed AMI conducted at March 5th at the Cardiology Department at Menoufia University Hospital with a first episode of acute myocardial infarction needing percutaneous coronary intervention (PCI).

Eligible participants were adults aged 18 years or older who presented with chest pain suggestive of AMI within six hours of symptom onset. Cases have been excluded if they had a history of previous myocardial infarction, severe hepatic or renal dysfunction, advanced heart failure, or a diagnosis of malignancy within the past five years.

Upon enrollment, all cases had a comprehensive clinical assessment. A detailed medical history was obtained, focusing on chest pain characteristics such as its quality, location, radiation, and associated symptoms like dyspnea, nausea, vomiting, diaphoresis, and syncope. Information regarding symptom relief with rest or nitroglycerin was also recorded. The physical examination assessed signs of systemic compromise, including skin pallor, peripheral or central cyanosis, diaphoresis, and abnormal pulse or blood pressure readings. Cardiac auscultation was performed to detect any abnormal heart sounds, particularly soft systolic murmurs.

A standard 12-lead electrocardiogram (ECG) was performed at rest to evaluate for AMI-related changes. ST-segment elevation ≥one millimeters in at least 2 contiguous leads and the existence of pathological Q waves were key diagnostic criteria. Serial ECGs were obtained every eight hours over a 24-hour period to monitor for evolving changes.

Blood samples were collected at various times throughout the day and night, ranging from 12:00 AM to 10:30 PM, to accommodate patients' surgical schedules. The majority of samples were taken in the preoperative period, with a smaller portion collected intraoperatively.

"Laboratory investigations included a complete blood count (CBC) and cardiac biomarkers like creatine kinase-MB (CK-MB), cardiac troponin I (cTnI), and serum copeptin levels. Serum copeptin was determined using a commercially available enzyme-linked immunosorbent assay (ELISA) kit (DLR-CPP-HU Human Copeptin [CPP] ELISA Kit, **DLD Diagnostika GmbH, Hamburg, Germany**) following the manufacturer's protocols.

Coronary angiography (CAG) was performed on all patients upon admission utilizing the standard Judkins method by experienced interventional cardiologists. Emergency PCI was initiated as soon as possible, particularly in cases diagnosed with ST-elevation myocardial infarction (STEMI), with efforts made to achieve a door-to-balloon time below ninety minutes. In cases where immediate PCI was unavailable, thrombolytic therapy was administered in accordance with established guidelines, targeting a door-to-needle time of thirty to sixty minutes.

The primary outcomes of the study included the association among serum copeptin and cTnI concentrations with the severity of coronary artery disease observed during angiography, as well as the diagnostic performance of copeptin in the early identification of acute myocardial infarction.

Statistical analysis has been conducted utilizing SPSS software, version 25.0. Continuous parameters have been expressed as mean ± standard deviation or median with interquartile range, based on data distribution, and have been compared using either independent t-test or Mann-Whitney U test. Categorical data have been represented as frequencies and percentages and examined utilizing the chi-square test. Receiver operating characteristic (ROC) curve analysis has been employed to evaluate the diagnostic utility of serum copeptin for early AMI detection, including specificity, sensitivity, and the area under the curve (AUC). A p-value less than 0.05 has been deemed statistically significant.

Ethical Considerations:

Ethical approval was granted by the local ethics committee of the Cardiology Department, Faculty of Medicine, Menoufia University, and written informed consent has been attained from all participants before their inclusion in the research. Prior to the participants have been admitted in this investigation, the nature and purpose of the research, in addition to the risk/benefit evaluation has been clarified to them. The study followed The Declaration of Helsinki through its execution.

RESULTS

Demographic Characteristics

The 2 study groups were similar regarding baseline demographic characteristics. The mean age was 45.2 ± 7.8 years in Group A and 44.6 ± 8.1 years in Group B, with no statistically significant variance. Gender distribution was also comparable, with males comprising 60% in Group A and 58% in Group B. Marital status didn't significantly vary among the groups, with the majority being married (70% in Group A and 66% in Group B) (**Table 1**).

Vital Signs at Presentation

Upon clinical presentation, participants in Group A had a significantly higher heart rate than those in Group B, as well as a significantly lower respiratory rate. However, diastolic and systolic blood pressure, along with body temperature, were not significantly different among the 2 groups (**Table 1**).

Table 1: Demographic and Vital Characteristics at Presentation

Variable	Group A (n = 50)	Group B (n = 50)	P-Value
Age (years)	**45.2 ± 7.8**	**44.6 ± 8.1**	**0.72**
Gender			
Male (%)	**30 (60%)**	**29 (58%)**	**0.84**
Female (%)	**20 (40%)**	**21 (42%)**	
Marital Status			
Married (%)	**35 (70%)**	**33 (66%)**	**0.68**
Single (%)	**15 (30%)**	**17 (34%)**	
Heart Rate (beats/min)	**88.4 ± 12.6**	**70.7 ± 11.9**	**<0.001***
Systolic BP (mmHg)	**124.2 ± 15.3**	**122.8 ± 14.6**	**0.63**
Diastolic BP (mmHg)	**78.5 ± 8.9**	**79.2 ± 9.2**	**0.76**
Respiratory Rate (breaths/min)	**18 ± 2.1**	**28 ± 2.0**	**<0.001***
Temperature (°C)	**37.1 ± 0.4**	**37.0 ± 0.5**	**0.58**

Data are presented as Mean ± SD or number (%), *: Significant

Ischemic Equivalents

Symptoms suggestive of ischemia were significantly more common among participants with acute myocardial infarction (AMI). Angina, dyspnea, palpitations, and fatigue were all reported at substantially higher rates in Group B in comparison with Group A. Syncope was also more common in the AMI group, while the difference in other symptoms didn't reach statistical significance (**Table 2**).

Cardiological Examination Findings

Physical examination findings associated with cardiac dysfunction were more frequently observed among AMI patients. Bilateral rales, wheezing, S3 heart sound, peripheral edema, and jugular venous distension were significantly more common in Group B in comparison with Group A (**Table 2**).

Table 2: Ischemic Equivalents and Cardiological Examination Findings

Parameter	Group A (n = 50)	Group B (n = 50)	P-Value
Angina	**8 (16%)**	**32 (64%)**	**<0.001***
Dyspnea	**10 (20%)**	**38 (76%)**	**<0.001***
Palpitations	**5 (10%)**	**18 (36%)**	**0.003***
Fatigue	**7 (14%)**	**26 (52%)**	**<0.001***
Syncope	**2 (4%)**	**8 (16%)**	**0.046***
Other Symptoms	**1 (2%)**	**5 (10%)**	**0.092**
Bilateral Rales	**2 (4%)**	**15 (30%)**	**<0.001***
Wheezing	**3 (6%)**	**12 (24%)**	**0.012***
S3 Heart Sound	**1 (2%)**	**10 (20%)**	**0.004***
Peripheral Edema	**3 (6%)**	**14 (28%)**	**0.003***
Jugular Venous Distension	**0 (0%)**	**8 (16%)**	**0.003***

*: Significant

Cardiac Risk Factors

Traditional cardiovascular risk factors were markedly more prevalent among AMI patients. These included hypertension, diabetes mellitus, hypercholesterolemia, and current or past smoking. Additionally, a positive family history of coronary artery disease and obesity were significantly more common in Group B (**Table 3**).

Table 3: Cardiac Risk Factors

Parameter	Group A (number = 50)	Group B (number = 50)	P-Value
Hypertension	**10 (20%)**	**32 (64%)**	**<0.001***
Diabetes Mellitus	**6 (12%)**	**26 (52%)**	**<0.001***
Hyper-cholesterolemia	**8 (16%)**	**30 (60%)**	**<0.001***
Smoking	**14 (28%)**	**35 (70%)**	**<0.001***
Family History of CAD	**9 (18%)**	**22 (44%)**	**0.005***
Obesity (BMI ≥30 kg/m²)	**15 (30%)**	**28 (56%)**	**0.009***

*: Significant.

Patients with acute myocardial infarction (Group B) had significantly lower hemoglobin levels and significantly higher white blood cell counts, and platelet counts compared to controls (Group A). Moreover, cardiac biomarkers including troponin I, CK-MB, and copeptin were markedly elevated in the AMI group with highly significant differences ($p < 0.001$). These findings indicate the reliability of copeptin in parallel with conventional cardiac biomarkers for distinguishing AMI patients from healthy individuals. **(Table 4).**

Table 4: Laboratory Findings

Parameter	Group A (n = 50)	Group B (n = 50)	P-Value
Hemoglobin (g/dL)	**13.8 ± 1.2**	**13.0 ± 1.5**	**0.004***
WBC (×10³/µL)	**7.2 ± 1.8**	**11.5 ± 2.4**	**<0.001***
Platelets (×10³/µL)	**220 ± 45**	**250 ± 60**	**0.006***
Troponin I (ng/L)	**3.0 (1.3)**	**180.0 (130)**	**<0.001***
CK-MB (U/L)	**16.0 (15)**	**120.0 (65)**	**<0.001***
Copeptin (pmol/L)	**4.5 (3.4)**	**588.18 (500)**	**<0.001***

Data are presented as Mean ± SD or as Median (IQR), *: Significant.

At a cutoff value of 104.5 pmol/L, copeptin achieved high sensitivity (88%) and specificity (84%), with balanced predictive values and overall diagnostic accuracy of 86%. The area under the ROC curve (AUC = 0.92, 95% CI: 0.88–0.96) confirms its strong discriminative power, supporting its role as an early and reliable biomarker for AMI diagnosis. **(Table 5).**

Table 5: Diagnostic Performance of Serum Copeptin for AMI

Parameter	Value
Best Cutoff Value (pmol/L)	**104.5**
Sensitivity (%)	**88.0**
Specificity (%)	**84.0**
Positive Predictive Value (%)	**85.0**
Negative Predictive Value (%)	**87.0**
Accuracy (%)	**86.0**
AUC (95% CI)	**0.92 (0.88–0.96)**

DISCUSSION

There are global burden and diagnostic challenges because of acute myocardial infarction, which remains a major etiology of morbidity and death globally according to **Roth *et al.*** [14]**.** Despite advances in diagnostic strategies and therapeutic interventions, early detection- particularly within the first hours following symptom onset-remains a challenge as mentioned in **Damen *et al.*** research [15].

In this initial window, cardiac troponin may remain within the reference range, delaying treatment initiation as shown in **Mair *et al.*** [16]. This limitation has led to exploration of novel biomarkers such as copeptin, a stable glycopeptide derived from the precursor of arginine vasopressin, which rises rapidly in response to acute physiological stress according to **Morgenthaler *et al.*** [17]**.**

Cardiovascular Risk Factors

Our findings revealed a significantly greater occurrence of traditional cardiovascular risk factors-hypertension, diabetes mellitus, hypercholesterolemia, smoking, and obesity-among AMI cases in comparison with controls. This is in agreement with previous studies linking these comorbidities to coronary artery disease [15,18].

For instance, **Damen *et al.*** emphasized the role of metabolic syndrome in increasing both AMI risk and adverse outcomes [15]**.**

Clinical Presentation

Typical ischemic symptoms such as chest pain, dyspnea, fatigue, palpitations, and syncope were more frequent among AMI patients, consistent with earlier studies as **Fekonja *et al.*** [19] and **Khan *et al.*** [20]**.** Although chest pain remains the hallmark presentation, atypical symptoms particularly in elderly and female patients complicate diagnosis. This highlights the need for adjunctive biomarkers to aid early and accurate detection.

Vital Signs and Physical Examination

Elevated respiratory and heart rates were observed in AMI patients, reflecting sympathetic activation and reduced cardiac output **as in Goyal *et al.*** [21] and **Brener *et al.*** [22]. No significant differences were found in systolic or diastolic blood pressures between groups, a result aligns with **Gąsecki *et al.*** [23]**,** who documented considerable variability based on comorbidities, medications, and infarct size.

On examination, signs of left ventricular dysfunction and fluid overload-such as bilateral basal crepitations, peripheral edema, jugular venous distension, and an audible S3 gallop-were more prevalent in AMI patients, consistent with prior reports of **Long and Koyfman** [24] and **Antman and Loscalzo** [25]**.**

Laboratory Findings

Significantly higher white blood cell and platelet counts have been noted in AMI patients, reflecting inflammatory and thrombotic activity associated with myocardial injury as shown by **Madjid *et al.*** [26] and **Furman *et al.*** [27]**.** These parameters have been linked to larger infarct size and worse clinical outcomes.

Regarding role of copeptin in early AMI diagnosis, our results demonstrated markedly elevated copeptin

levels in AMI patients (mean 588.18 pmoi/L) compared to controls (4.5 pmoi/L). Copeptin, co-released with arginine vasopressin, rises rapidly after ischemia and is more stable for measurement as shown by **Morgenthaler *et al.*** [17] and **Mu *et al.*** [28].

ROC analysis showed high diagnostic performance with sensitivity 88%, specificity 84%, and AUC 0.92, closely matching pooled results from **Mu *et al.*** [28].

Rapid elevation of copeptin by dual-marker diagnostic strategy, offers a distinct advantage over troponin, which may take hours to rise post-onset according to **Maisel *et al.*** [29]. Combining copeptin with troponin significantly enhances early diagnostic accuracy, particularly within the first three hours as was shown by **Kankra *et al.*** [30]. **Mueller-Hennessen *et al.*** [31] demonstrated that this dual-marker approach can reliably rule out NSTEMI in low-to-intermediate risk patients, potentially reducing unnecessary admissions and improving emergency department efficiency.

CONCLUSION

Our study provides compelling evidence that serum copeptin is a powerful and rapid diagnostic tool for acute myocardial infarction (AM1), particularly during the critical early window when timely intervention can save myocardium and lives. Unlike cardiac troponin, which may require 3-6 hours after symptom onset to rise above diagnostic thresholds, copeptin levels increase sharply within minutes- often detectable at clinically significant levels in less than one hour. When combined with troponin in a dual-marker strategy, it can dramatically shorten the diagnostic process, reduce unnecessary hospital admissions, and expedite initiation of life-saving therapies. These findings position copeptin as a promising candidate for incorporation into standard AMI diagnostic protocols. Future large-scale, multicenter trials are warranted to confirm its role, refine its cutoff thresholds, and potentially establish it as a priority biomarker for the earliest possible recognition of acute myocardial infarction.

DECLARATIONS

Consent for publication: I certify that each author has granted permission for the work to be submitted.
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