Article

Discovery Medicine 2024; 36(182): 598–603
https://doi.org/10.24976/Discov.Med.202436182.56

The Value of Combined Detection of Serum BNP, Cardiac Troponin-I and Dynamic Electrocardiogram in Early Clinical Diagnosis and Prognosis of Patients with Acute Myocardial Infarction

Qinxia Yu[1,*], Shuyan Yu[2]

[1]Electrocardiogram Room, The First People's Hospital of Chun'an County, 311700 Hangzhou, Zhejiang, China
[2]Department of Cardiology, The First People's Hospital of Chun'an County, 311700 Hangzhou, Zhejiang, China
*Correspondence: yuqinxia850569@163.com (Qinxia Yu)
Published: 20 March 2024

Background: Acute myocardial infarction (AMI) is a prevalent cardiovascular disease resulting from myocardial ischemia and necrosis due to coronary artery occlusion. AMI is characterized by a sudden onset and high mortality, underscoring the significance of early diagnosis and treatment for improving patient prognosis. This study endeavors to assess the utility of a combined assessment involving serum brain natriuretic peptide (BNP), cardiac troponin-I (cTnI), and dynamic electrocardiogram (ECG) in the early clinical diagnosis and prognosis prediction of AMI.

Methods: This paper constitutes a retrospective study. All enrolled patients underwent dynamic ECG examination. The study compared the serum levels of BNP and cTnI, along with pertinent dynamic ECG parameters [turbulence slope (TS) and standard deviation (SDNN) of the 24-hour interval between normal atrial depolarization and ventricular depolarization (R-R)], between the observation group (AMI patients) and the control group (patients with unstable angina (UA)). To evaluate the early diagnostic potential of AMI, we utilized receiver operating characteristic (ROC) curves to analyze serum BNP, cTnI, dynamic ECG, and their combined utility. Furthermore, a follow-up period of 6 months was conducted for AMI patients to record major adverse cardiovascular events (MACE).

Results: In the observation group, the serum levels of BNP and cTnI were significantly higher than those in the control group ($p < 0.001$), while dynamic ECG parameters, specifically TS and SDNN, were significantly lower in the observation group compared to the control group ($p < 0.001$). The results obtained from the ROC curve analysis revealed that the area under the curve (AUC) for BNP, cTnI, dynamic ECG, and their combination in early AMI diagnosis were 0.838, 0.887, 0.874, and 0.974, respectively. The 95% confidence intervals (CI) were 0.781~0.884, 0.836~0.926, 0.822~0.915, and 0.942~0.991, respectively. Sensitivity values were 64.29%, 82.14%, 91.07%, and 88.39%, and specificity values were 91.00%, 88.00%, 70.00%, and 98.00%, respectively. Significantly, the combination of all three markers demonstrated superior efficacy in early AMI diagnosis compared to any single index ($p < 0.05$). During the 6-month follow-up of 112 AMI patients, 22 experienced MACE. The MACE group exhibited notably higher serum BNP and cTnI levels compared to the non-MACE group. Additionally, dynamic electrocardiogram parameters TS and SDNN demonstrated a significant decrease ($p < 0.05$) in the MACE group.

Conclusions: The combined assessment of serum BNP, cTnI, and dynamic electrocardiogram enhances the early clinical diagnostic potential for AMI and holds value in assessing the prognosis of AMI patients.

Keywords: acute myocardial infarction; brain natriuretic peptide; cardiac troponin-I; dynamic electrocardiogram; diagnostic value; prognostic analysis

Introduction

Acute myocardial infarction (AMI) is a prevalent cardiovascular disease, primarily caused by myocardial ischemia and necrosis resulting from coronary artery occlusion [1]. Patients with AMI typically manifest characteristic electrocardiographic changes, such as acute circulatory dysfunction, severe and persistent chest pain, along with elevated serum myocardial enzymes [2,3]. Given its abrupt onset and high mortality rate, early diagnosis and prompt treatment of AMI are of paramount importance for patient prognosis. Clinical diagnosis of AMI commonly relies on serological markers and electrocardiograms. Among these, cardiac troponin-I (cTnI) stands out as a crucial indicator of myocardial injury, closely associated with the extent of the damage, making it a pivotal serum marker for the clinical diagnosis of AMI [4]. While cTnI boasts high sensitivity in AMI diagnosis, it's important to note that myocardial damage can also occur in other clinical scenarios, such as severe infections or trauma, which may lower the speci-

ficity of cTnI. Therefore, it becomes imperative to comprehensively assess the presence of AMI by considering other clinical manifestations and diagnostic examinations [5]. Brain natriuretic peptide (BNP) is a neurohormone secreted by ventricular myocytes and released into the systemic circulatory system when the ventricle undergoes dilation or experiences pressure overload [6]. Notably, BNP levels demonstrate a rapid increase within the first 24 hours following an acute myocardial infarction, followed by a tendency to stabilize. This characteristic renders BNP a valuable indicator for predicting the extent of ischemic injury and damage to left ventricular function [7]. Dynamic electrocardiogram (ECG) stands as an advanced cardiac electrophysiological monitoring technique, capable of continuous ECG signal recording over 24 hours and providing multilead data [8]. Such examinations offer physicians a scientifically grounded approach to enhance the accuracy of diagnosis and prognosis evaluation for various diseases. In light of these considerations, this study conducted an analysis of the combined assessment of serum BNP, cTnI, and dynamic ECG in the context of early clinical diagnosis and prognosis assessment of AMI, shedding light on its practical applications in clinical settings.

Materials and Methods

Design and Procedures

A total of 112 AMI patients who were admitted to our hospital between May 2020 and January 2023 were selected as the observation group. In addition, 100 patients diagnosed with unstable angina (UA) were chosen as the control group for this retrospective study. The purpose of this study was to compare the observation group consisting of AMI patients, with the control group consisting of patients with unstable angina (UA) pectoris, who were admitted during the same period. The assessment involved comparing the levels of serum BNP and cTnI, as well as related dynamic ECG parameters, which included turbulence slope (TS) and the standard deviation (SDNN) of the 24-hour interval between normal atrial depolarization and ventricular depolarization (R-R).

Setting and Participants

The eligibility and exclusion criteria for patients were assessed based on their inclusion status. Following a meticulous screening process, the participants were randomly assigned. Inclusion criteria encompassed the following: (1) Age ranging from 40 to 75 years; (2) Meeting the clinical diagnostic criteria for AMI and UA as outlined in references [9,10], which included having at least two of the following three criteria: a clinical history of ischemic chest pain, dynamic evolution of the electrocardiogram, and dynamic changes in serum myocardial marker concentration indicative of myocardial necrosis; (3) Availability of complete clinical data; (4) Demonstrating good compliance and a commitment to follow-up. On the other hand, exclusion criteria included: (1) Patients with severe hepatic or renal insufficiency; (2) Patients with a history of brain trauma or other cerebrovascular diseases; (3) Patients with infections or immune system disorders; (4) Patients diagnosed with malignant tumors. No subjects were dropped from the study, and approval for this research was granted by the hospital's ethics committee.

Observation Indexes

Sample Collection and Testing

Upon admission, 5 mL of fasting venous blood was collected from all patients in the morning. Following centrifugation, the supernatant was carefully collected and subsequently stored in a freezer at –80 °C. Serum BNP and cTnI expression levels were assessed using electrochemiluminescence, and the procedure was executed in accordance with the provided instructions.

Treatment Procedure

All patients underwent percutaneous coronary intervention (PCI) treatment and received oral administration of 300 mg aspirin (Shandong Xinhua Pharmaceutical Co., Ltd., Shandong, China, Sinopharmate code: H37022905) and 300 mg clopidogrel (Shenzhen Xinritai Pharmaceutical Co., Ltd., Shenzhen, China, H20120018). Intraoperatively, a 10,000 U dose of regular heparin (Wuhan Biochemical Pharmaceutical Co., Ltd., Wuhan, China, Sinopharmary code: H20123352) was administered. The embolized arteries were located based on the placement of ECG leads and the extent of vascular blockage. Balloons appropriate for the patient's specific conditions were chosen to dilate constricted and occluded lumens. This was followed by intravascular stent implantation, with post-dilation assessments, including evaluating residual stenosis, distal coronary artery blood flow, and the presence of intimal dissection or tears. Throughout the procedure, close monitoring of the patient's heart rate and blood pressure, as well as vigilant observation of changes in ultrasound electrocardiograms, were maintained. Any patient issues were promptly identified and addressed with symptomatic treatment. Following surgery, patients were placed on oral doses of clopidogrel and aspirin, both at 75 mg per day, in addition to a 7-day course of heparin injections (5000 U). Surgical success criteria included local residual stenosis $<20\%$, a thrombolysis in myocardial infarction (TIMI) blood flow rating of grade 3, and the absence of PCI-related complications.

Dynamic ECG Detection

In AMI patients, holter electrocardiography is not routinely performed prior to PCI. Instead, a 12-lead dynamic ECG was utilized for patient assessment, allowing them to be in either a standing or sitting position. Before attaching the necessary electrodes, the skin areas were meticulously cleaned with 75% alcohol-soaked gauze. These areas

Table 1. Baseline characteristics in two groups ($\bar{x} \pm s$).

Grouping	Observation group (n = 112)	Control group (n = 100)
Males	67	55
Females	45	45
Average age	66.83 ± 9.47	66.12 ± 9.04
Smoking (cases)	42	38
Hypertension (cases)	74	61
Diabetes mellitus (cases)	28	25
Hyperlipidemia (cases)	35	30

Table 2. Serum levels of BNP and cTnI in two groups ($\bar{x} \pm s$).

Grouping	BNP (pg/mL)	cTnI (pg/L)
Observation group (n = 112)	161.73 ± 63.28	2.20 ± 0.68
Control group (n = 100)	97.64 ± 28.82	0.87 ± 0.33
t	9.302	17.776
p	<0.001	<0.001

BNP, brain natriuretic peptide; cTnI, cardiac troponin-I.

encompassed the anterior chest, subclavian fossa, bilateral upper limbs, bilateral lower limbs, and the region bilaterally subcostal, approximately 1 cm from the midline of the clavicle. Following proper skin preparation, the electrode pieces were secured, and the patient wore the ECG recorder. ECG signals were continuously recorded from 8:00 am to 8:00 am the following day, providing a full 24-hour dataset. Subsequently, various indicators such as turbulence slope (TS) and the standard deviation (SDNN) of the 24-hour interval between normal atrial depolarization and ventricular depolarization (R-R) were meticulously analyzed.

Follow-up

The follow-up duration extended for a period of 6 months, during which no attrition of clinical patients occurred. Throughout this follow-up period, the incidence of major adverse cardiovascular events (MACE) [11] was diligently recorded among AMI patients. Subsequently, patients were categorized into two distinct groups, namely the MACE group and the non-MACE group, based on the occurrence of these adverse events. A comprehensive analysis was then conducted to investigate the correlations between serum BNP, cTnI, Holter monitor parameters, and the presence of MACE.

Statistics

SPSS 27.0 software (IBM Corp., Armonk, NY, USA) was used to analyze the data. The measurement data were consistent with normal distribution and the variance was uniform, expressed by $\bar{x} \pm s$. The comparison between the two groups was tested by independent sample t value. The counting data was represented by [n (%)] and tested using χ^2. The diagnostic value of serum BNP, cTnI, Holter monitor and their combination in the early stage of AMI was analyzed by receiver operating characteristic (ROC) curve; The difference with $p < 0.05$ was statistically significant.

Table 3. Two groups of dynamic ECG parameters ($\bar{x} \pm s$).

Grouping	TS (ms/RRI)	SDNN (ms)
Observation group (n = 112)	1.92 ± 0.80	68.64 ± 16.17
Control group (n = 100)	3.10 ± 1.19	91.22 ± 19.44
t	8.552	9.227
p	<0.001	<0.001

ECG, electrocardiogram; TS, turbulence slope; RRI, R-R intervals; SDNN, standard deviation.

Results

Basic Data and Serum BNP and cTnI Levels

In the observation group, there were 67 male and 45 female patients, with an average age of (66.83 ± 9.47) years, ranging from 40 to 75 years. Additionally, 42 of them had a history of smoking, 74 had hypertension, 28 had diabetes mellitus, and 35 had hyperlipidemia. In the control group, there were 55 male and 45 female patients, with an average age of 66.12 ± 9.04 years, within the age range of 42 to 75 years. Among them, 38 had a history of smoking, and there were 61 cases of hypertension, 25 cases of diabetes, and 30 cases of hyperlipidemia. There were no significant differences in terms of gender, age, smoking history, and the presence of comorbidities between the two groups ($p > 0.05$). See Table 1. However, in comparison to the control group, the observation group exhibited significantly higher levels of serum BNP and cTnI ($p < 0.0.001$) (refer to Table 2).

Dynamic ECG Parameters

Versus the control group, the dynamic ECG parameters TS and SDNN of the observation group were lower ($p < 0.001$) (Table 3).

The Efficacy of Serum BNP, cTnI, Dynamic Electrocardiogram and Combined Detection in the Early Diagnosis of AMI

The ROC curve analysis revealed that the area under the curve (AUC) for serum BNP, cTnI, and dynamic ECG in the early diagnosis of AMI were 0.838, 0.887, and 0.874, respectively. Notably, when all three markers were combined for diagnosis, the AUC value reached an impressive 0.974. The 95% confidence intervals (CI) for these AUC values were 0.781~0.884, 0.836~0.926, 0.822~0.915, and 0.942~0.991, respectively. The corresponding sensitivities were 64.29%, 82.14%, 91.07%, and 88.39%, while specificities were 91.00%, 88.00%, 70.00%, and 98.00%, in the same order. Importantly, the combined diagnosis of AMI exhibited significantly superior efficacy compared to the individual markers of BNP, cTnI, and dynamic ECG ($p < 0.05$) (refer to Table 4 and Fig. 1).

Table 4. The efficacy of serum BNP, cTnI, dynamic ECG and combined detection in the early diagnosis of AMI.

Indexes	Cutoff	AUC	Youden index	95% CI	Sensitivity	Specificity
BNP	136.66 pg/mL	0.838	0.553	0.781~0.884	64.29	91.00
cTnI	1.19 pg/L	0.887	0.701	0.836~0.926	82.14	88.00
Dynamic ECG	/	0.874	0.611	0.822~0.915	91.07	70.00
Combination of the three	/	0.974	0.864	0.942~0.991	88.39	98.00

AMI, Acute myocardial infarction; AUC, area under the curve; CI, confidence intervals.

Table 5. Serum BNP, cTnI and dynamic electrocardiogram parameters in MACE group and non-MACE group ($\bar{x} \pm s$).

Grouping	BNP (pg/mL)	cTnI (pg/L)	TS (ms/RRI)	SDNN (ms)
MACE group (n = 22)	195.26 ± 75.14	2.75 ± 0.73	1.67 ± 0.65	60.55 ± 14.36
Non-MACE group (n = 90)	153.53 ± 68.70	2.07 ± 0.59	1.98 ± 0.64	70.62 ± 18.13
t	2.507	4.618	2.031	2.423
p	0.014	<0.001	0.045	0.017

MACE, major adverse cardiovascular events.

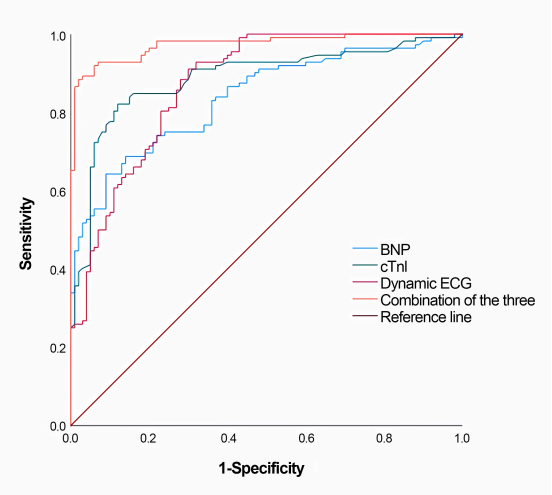

Fig. 1. Receiver operating characteristic (ROC) curve of serum BNP, cTnI, dynamic electrocardiogram and combined detection in the diagnosis of early AMI.

Occurrence of Major Cardiovascular Adverse Events in Patients with AMI

Throughout the 6-month follow-up period, 22 AMI patients experienced MACE, designating them as the MACE group. These events included 7 cases of angina pectoris, 10 cases of recurrent myocardial infarction, and 2 cases of heart failure. In contrast, 90 patients in the non-MACE group did not encounter MACE. It's noteworthy that when comparing the two groups, the MACE group exhibited higher levels of serum BNP and cTnI, along with lower values for dynamic ECG parameters TS and SDNN ($p < 0.05$) (refer to Table 5).

Discussion

The pathogenesis of AMI primarily stems from coronary atherosclerosis, which results in the obstruction of coronary blood flow due to thrombosis. This, in turn, swiftly diminishes the blood supply to cardiomyocytes, leading to ischemic necrosis of these heart muscle cells [12,13]. Furthermore, a sharp increase in oxygen demand by cardiomyocytes and the possibility of coronary artery spasms can also contribute to ischemic necrosis [14,15]. The hallmark symptoms of AMI patients often encompass persistent and severe chest pain, accompanied by elevated body temperature. In severe instances, patients may experience arrhythmias, heart failure, and, in the most critical cases, even shock. Notably, chest pain is the predominant initial symptom of angina pectoris in the early stages of AMI, which can potentially lead to the underdiagnosis or misdiagnosis of AMI patients, thereby impacting their prognosis [16]. Hence, the importance of early diagnosis and treatment for AMI cannot be overstated. These measures have the potential to reduce myocardial necrosis, decrease the likelihood of complications, and ultimately enhance the prognosis of AMI patients.

The results of the study indicated that the levels of serum BNP and cTnI in the observation group were significantly higher compared to the control group. Additionally, the parameters TS and SDNN in the observation group were notably lower than those in the control group. These findings underscore the potential of serum BNP, cTnI, and dynamic ECG as valuable tools for the early diagnosis of AMI. BNP, a hormone produced by ventricular myocytes, serves a dual role by not only inhibiting the renin-angiotensin-aldosterone system but also promoting the dilation of glomerular arteries and blood vessels [17]. When AMI occurs, the myocardium undergoes ischemic and necrotic changes, leading to reduced contractility and decreased compliance. Consequently, myocardial stretching, elevated heart rate, and increased atrial and ventricular volume and wall tension load ensue. In response to this negative feedback, the body initiates the synthesis and secretion of substantial amounts of BNP [18].

A related study [19] has demonstrated a positive correlation between the increase in serum BNP levels and the

size and severity of myocardial infarction. Notably, even before abnormal left ventricular systolic function manifests in patients with non-ST segment elevation myocardial infarction, their serum BNP levels significantly rise. This suggests that BNP is intricately linked to the early stages of myocardial infarction and can serve as an adjunct diagnostic indicator for early AMI [20]. In contrast, cTnI stands as a commonplace serum marker for clinically detecting myocardial cell injury, playing a pivotal role in the diagnosis of AMI [21,22]. Furthermore, 24-hour dynamic ECG has become a common clinical cardiology examination method in recent years. Previous studies have unveiled a substantial correlation between the heart rate turbulence index TO and TS, and the degree of coronary artery disease. Among these, TS exhibits the strongest correlation and can serve as an effective indicator for predicting the extent of coronary artery disease and identifying high-risk patients [23]. Additionally, SDNN, a parameter of heart rate variability, represents a crucial index reflecting the equilibrium between sympathetic and vagus nerve activity, and is associated with myocardial injury in AMI patients [24]. Both TS and SDNN hold valuable reference value in AMI diagnosis, consistent with the outcomes of prior research [25].

In this study, the ROC curve analysis revealed that the AUC values for serum BNP, cTnI, and dynamic ECG in the early diagnosis of AMI were 0.838, 0.887, and 0.874, respectively. These results indicate that they can be utilized as reliable indicators for the early diagnosis of AMI. Furthermore, when these three markers were combined for diagnosis, the AUC value significantly increased to 0.974, yielding a sensitivity of 88.93% and a specificity of 98.00%. This suggests that combining serum BNP and cTnI with dynamic ECG can enhance the specificity and diagnostic accuracy in the early diagnosis of AMI. Studies have demonstrated that the rate of BNP increase is most rapid within the first 12 to 20 hours of the early stages of AMI. Afterward, this increase slows down between 20 to 24 hours, eventually peaking at the 24-hour mark following the onset of symptoms [26,27]. Hence, BNP holds substantial value in the early diagnosis of AMI. It is well-established that myocardial injury in AMI patients occurs subsequent to myocardial ischemia. Therefore, the increase in serum cTnI levels tends to lag behind BNP, but it persists for a relatively longer duration. However, it's important to note that myocardial injury induced by factors other than AMI can also result in elevated cTnI levels. As such, cTnI is not generally employed as a standalone early diagnostic marker for AMI [28,29]. Moreover, AMI can contribute to a decrease in heart rate variability, which subsequently leads to reduced sympathetic nerve activity and tension, along with a decrease in TS and SDNN [30]. Consequently, combining dynamic ECG detection with serum markers BNP and cTnI results in a more comprehensive and precise early diagnosis of AMI, thus enhancing its clinical diagnostic value.

Furthermore, this study has also uncovered notable differences in serum BNP, cTnI levels, and dynamic ECG parameters TS and SDNN among AMI patients with varying prognoses. The levels of serum BNP and cTnI in the MACE group are significantly higher than those in the non-MACE group, while TS and SDNN are significantly lower. These findings indicate that serum BNP, cTnI, and dynamic ECG can also serve as indicators of AMI prognosis, which aligns with the conclusions drawn by Xin XW *et al*. [31].

Conclusions

In conclusion, the combined detection of serum BNP, cTnI, and dynamic ECG holds significant value in both the early diagnosis and prognosis evaluation of AMI. Significantly, the combination of all three markers demonstrated superior efficacy in early AMI diagnosis compared to any single index.

Availability of Data and Materials

The data used to support the findings of this study are available from the corresponding author upon request.

Author Contributions

QXY contributed to the conception of the study and performed the study. SYY helped to collect the data and performed data collection and manuscript preparation with constructive suggestions. QXY and SYY wrote the manuscript. Both authors are responsible for all aspects of their work, ensuring that issues relating to the accuracy or completeness of any part of their work are properly investigated and resolved. Both authors have reviewed and approved the manuscript.

Ethics Approval and Consent to Participate

This study has been approved by the ethics committee of The First People's Hospital of Chun'an County (2023-04-12-19), in compliance with the Declaration of Helsinki. All patients and their families give informed consent.

Acknowledgment

Not applicable.

Funding

This research received no external funding.

Conflict of Interest

The authors declare no conflict of interest.

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