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STUDY OF SERUM PERIOSTIN CONCENTRATION IN PREDICTING CARDIAC FUNCTION AFTER ACUTE MYOCARDIAL INFARCTION

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INTRODUCTION

1. RATIONALE FOR THE RESEARCH

There are up to 3 million people in the world who have myocardial infarction and 1 million Americans die each year from myocardial infarction [111]. The work of assessing the risk and prognosis of patients with acute myocardial infarction plays an important role. In that general trend, periostin - an inflammatory biomarker promises to be an effective and necessary factor in accurately predicting the disease's course in recent times.

In the world, the periostin is increasingly studied. Since the 2010s, using periostin to predict the severity of the damage after myocardial infarction has been carried out not only in Europe but also Asian countries. In Vietnam, there is currently no author studying the predictive role of periostin about cardiac function after acute myocardial infarction.To contribute to a more comprehensive assessment of the role of periostin in the prediction of cardiac function after myocardial infarction, we implemented ***"Study of serum periostin concentration in predicting cardiac function after acute myocardial infarction".***

2. RESEARCH OBJECTIVES

1. Survey of clinical and paraclinical characteristics and serum periostin concentration in patients after acute myocardial infarction.

2. Evaluation the relationship between serum periostin concentration with NT-proBNP, left ventricular ejection fraction, GRACE score, MESA heart failure prediction score and the predictive value of cardiac systolic function of periostin after 3 months.

3. CONTRIBUTIONS OF THE RESEARCH

In Vietnam, there has been no study on periostin in predicting cardiac systolic function after acute myocardial infarction. The thesis has practical and scientific significance in clinical practice. This study

demonstrated the value of periostin in providing important prognostic information, contributing to risk stratification. The study provided sensitivity, specificity, positive predictive value, negative predictive value, ROC curve, and cut-off point of serum periostin in predicting cardiac systolic function after myocardial infarction 3 months.

Research on periostin is a new biomarker that helps clinicians accurately assess the prognosis of cardiac complications after acute myocardial infarction, so that promptly and effectively treat patients, improve quality of life, and prolong life for patients. Periostin can be combined with other factors such as GRACE and MESA scores in predicting the outcome of patients after acute myocardial infarction.

4. THESIS STRUCTURE

The thesis comprises 138 pages (not including the references and appendices), is divided into:

- Introduction: 4 pages
- Chapter 1. Overview: 36 pages
- Chapter 2. Study subjects and research methods: 32 pages
- Chapter 3. Research results and findings: 31 pages
- Chapter 4. Disccussions: 32 pages
- Conclusion: 1 pages
- Petition: 1 page
- Limit: 1 page

The thesis includes: 57 tables, 18 images, 4 diagrams, 14 charts and 174 references including 22 in Vietnamese and 152 in English.

Chapter 1
OVERVIEW

1.1. OVERVIEW OF ACUTE MYOCARDIAL INFARCTION
1.2. BIOLOGICAL MARKERS IN ACUTE MYOCARDIAL INFARCTION
1.3. OVERVIEW OF PERIOSTIN
1.3.1. Origin of periostin

Discovered in 1993 in the periosteum, it is also found in other organs such as the kidney, lung, and heart valves of adult mammals.

1.3.2. Effects of periostin on the heart

Periostin participates in the remodeling process in heart development [48], is a protein that stimulates the proliferation of cardiomyocytes, causing the re-establishment of the cell cycle of cardiomyocytes [91], [92]. If periostin is overproduced in the heart, it will lead to cardiac dysfunction, significantly increasing fibrosis.

1.3.3. Effects of periostin in acute myocardial infarction

Periostin may accelerate cellular injury in myocardial infarction by promoting programmed cell death.

1.4. ASSESSMENT OF CARDIAC FUNCTION AFTER MYOCARDIAL INFARCTION
1.4.1. Some methods of assessing cardiac function:

- Echocardiography.
- Speckle tracking echocardiography.
- Myocardial perfusion imaging.
- Cardiac magnetic resonance imaging.
- Exercise test.
- Angioplasty.

1.4.2. The role of echocardiography in the prognosis of cardiac function

Post-AMI left ventricular remodeling is characterized by changes in size, shape, and function as a result of myocardial injury

or stress [9]. This process usually begins within hours of infarction and progresses over time. Thinning and dilation of the infarcted area after MI is defined as infarct expansion and usually results in changes in left ventricular shape, volume and loss of function gradually. With remodeling, the dilated left ventricle assumes a nearly spherical shape and is functionally impaired.

Echocardiography is a non-invasive method commonly used after MI, related to the prognosis of heart failure, helping to evaluate the left ventricular structure after MI, including assessing the ejection fraction, size, shape and volume of the left ventricle at the end of systole and diastole [9]. Echocardiography helps to examine the morphology, function and hemodynamics of the heart chambers, heart wall, pericardium and large blood vessels connected to the heart, measuring the necessary indicators in assessing heart function such as LVEF: (LVEF (%) = (EDV - ESV)/ EDV x 100 [94]), LVEDD (average in men is 50.2 mm, in women is 45.0 mm) or LVESD (average in men is 32.4 mm, in women is 28.2 mm) [94].

RELATED STUDIES

Some relatedly published studies:

In 2012, Chi-Wen Cheng et al. studied 123 people, patients were measured for NT-proBNP, and echocardiography was performed 3 months after myocardial infarction [42]. The results showed that acute myocardial infarction was associated with changes in blood periostin levels and periostin was used to predict cardiac function 3 months after myocardial infarction.

In 2014, Lin Ling et al. followed up on 50 patients with ST elevation myocardial infarction and found that serum periostin levels were inversely correlated with LVEF and LAD, and positively correlated with Killip grading [100]. The 6-month follow-up showed that patients with higher blood periostin levels had worse disease severity.

S. Andrup et al reported at the European Society of Cardiology 2022 that higher periostin concentrations were associated with a greater risk of death and suggested that periostin could be used as a prognostic tool in ischemic injury [27].

At the ESC Acute Cardiovascular Care 2022 conference, Ioana-Patricia Rodean et al. showed that higher blood periostin concentrations correlated with larger myocardial infarction zone and more severe clinical outcomes in patients with acute coronary syndrome and periodontal disease [133].

Currently, in Vietnam, there is no research on the role of periostin in predicting cardiac function after AMI.

Chapter 2
PATIENTS AND METHODS

2.1. PATIENTS

Patients were diagnosed acute myocardial infarction at Hue Central Hospital and Trieu An – Loan Tram Hospital since September 2019 until March 2023. Patients were follow up 3 months after AMI. Control group was also collected during this same period.

• Inclusion criteria

- Patient was diagnosed AMI.
- Agree to participate in the study.

• Exclusion criteria

- Moderate to severe valvular heart disease.
- Concurrent inflammation.
- Malignancy disease.
- Hypertrophic cardiomyopathy.
- Dilated cardiomyopathy.
- Serum creatinine ≥ 4 mg/dL (353.6 μmol/L) [42].

2.2. RESEARCH METHODS

2.2.1. Research design

Our study was a cross-sectional descriptive study with a control group. Sample size: N ≥ 122 patients. Sampling is non-probability, purposeful.

2.2.2. Research implementation steps

- History taking.
- Clinical and paraclinical examination.

2.2.3. Techniques performed during the research process

- Electrocardiogram.
- Echocardiogram: at admission and 3 months after AMI.
- Coronary angiography.
- Blood tests: glucose, lipid profile, urea, creatinine, troponin Ths, blood count. Periostin and NT-proBNP tests during hospitalization and 3 months after MI.

2.2.4. Periostin quantification technique

The patient's serum sample is taken into a test tube without anticoagulant. The sample will be centrifuged immediately after collection. If it cannot be done immediately, it must be stored at -20^{o}C. The first time is 5-7 days after MI, when the periostin concentration peaks.

2.2.5. Some diagnostic criteria used in the study

- Classification of angina pectoris [1].
- Diagnostic criteria for hypertension: according to ESC/ESH 2018 [164].
- Diagnostic criteria for obesity: according to WHO 2000 [163].
- Dyslipidemia: according to NCEP [118].
- Diagnostic criteria for acute MI: according to ESC 2017 [158].
- Diagnostic criteria for ST elevation in acute MI.
- Diagnosis of heart failure: according to ESC 2016 [128].

2.2.6. Cardiovascular risk scores in the study

Including the Gensini, SYNTAX I, SYNTAX II, GRACE and MESA scores.

Chapter 3
RESULTS

From September 2019 to March 2023, we collected data from 153 AMI patients, followed up after 3 months and 153 people as a control group at Hue Central Hospital and Trieu An - Loan Tram Hospital, we came to these results:

3.1. GENERAL CHARACTERISTICS OF THE STUDY SAMPLE

3.1.1. Demographics

- Group < 60 years old: 19.00%, group 60 - 69 years old: 34%, 70 - 79 years old: 20.90% and ⬝ 80 years old: 26.10%. The youngest age was 38 years old and the oldest age was 96 years old. Average age: 70.29 ± 12.23 years old.

- Male: 60.13%; female: 39.87%. Male/female ratio is 1.5.

3.1.2. Risk stratification according to cardiovascular risk scores

There was a difference in cardiovascular risk scores of GRACE and MESA score between the two AMI groups of ST elevation and non-ST elevation.

3.2. CLINICAL, PARACLINICAL CHARACTERISTICS AND SERUM PERIOSTIN CONCENTRATION IN AMI PATIENTS

3.2.1. Clinical characteristics

3.2.1.1. Characteristics of angina on admission to hospital

Table 3.5. *Characteristics of angina on admission to hospital*

Characteristics of angina		**Total (n = 153)**
		n (%)
Have chest pain		147 (96,08)
Typical angina		130 (84,97)
Reason for hospitalization	Angina	134 (87,58)
	Other	19 (12,42)

3.2.1.2. Unusual clinical features on admission

Table 3.7. *Unusual clinical features on admission*

Unusual clinical		**n**	**%**
Fast pulse (> 100 times/minute)		47	30,72
Systolic hypertension		67	43,79
Diastolic hypertension		43	28,10
Hypertension		76	49,67
Hypertension	Grade I	38	50,00
	Grade II	27	35,53
	Grade III	11	14,47

3.2.2. Paraclinical features

3.2.2.1. NT-proBNP at admission and 3 months after AMI

Table 3.8. *NT-proBNP at admission and 3 months after AMI*

NT-proBNP (mg/dL)	**ST elevation**	**Non-ST elevation**	**p**
	Median (Interquartile range)	**Median (Interquartile range)**	
At admission	699,00 (131,00 - 1762,00)	770,50 (255,50 - 3734,00)	0,054
After 3 months	677,00 (312,00 - 2846,00)	1163,50 (322,75 - 4484,00)	0,233
NT-proBNP	**At admission**	**After AMI 3 months**	**p**
	813,00 (199,00 - 3739,00)	897,00 (319,00 - 4126,50)	0,051

3.2.2.2. Echocardiography

Table 3.13. LVEF on admission in groups with a history of heart failure *(n = 45)*

LVEF (%)	**History of heart failure**	
	n	**%**
≥ 50	30	66.67
40 - 49	10	22,22
< 40	5	11,11
Total	45	100,00

The majority of acute MI patients with a history of heart failure in this study had preserved or mildly reduced LVEF.

Table 3.15. *Echocardiography at admission and after AMI 3 months*

Echocardiography parameters			**p value**
LVEF (%)	At admission	53,42 ± 13,13	**0,001***
	After AMI 3 months	49,37 ± 10,43	
LAD (mm)	At admission	31,34 ± 4,52	**0,038***
	After AMI 3 months	31,76 ± 3,87	
LVESD (mm)	At admission	36,18 ± 8,84	**< 0,001***
	After AMI 3 months	39,52 ± 7,05	
LVEDD (mm)	At admission	50,49 ± 7,85	**< 0,001***
	After AMI 3 months	54,95 ± 8,73	

There were differences in LVEF, LAD, LVESD and LVEDD parameters on echocardiography at admission and 3 months after MI.

3.2.3. Serum periostin concentrations in AMI patients

3.2.3.1. Periostin concentrations in the case and control groups

Table 3.17. *Periostin concentrations in the case and control groups*

Periostin (ng/mL)		**n**	**Median (Interquartile range)**	**p**
Disease group 1 st time	Male	92	142,41 (117,17 – 203,56)	0,236*
	Female	61	156,00 (124,04 - 218,01)	
Disease group 2 nd time	Male	92	73,61 (59,07 – 97,20)	0,158*
	Female	61	78,61 (66,74 – 112,63)	
Control group	Male	92	65,76 (36,14 – 80,71)	0,579*
	Female	61	60,66 (42,33 – 81,09)	
Compare	1st time [a]		149,37 (120,69 – 208,18)	$p^{(a-b)}$ < **0,001****
	2nd time [b]		77,69 (61,63 – 101,05)	
	Control group[c]		63,04 (40,96 – 80,98)	$p^{(a-c)}$ < **0,001*** $p^{(b-c)}$ < **0,001***

Serum periostin concentration of the first-tested patient group > periostin concentration of the second-tested patient group > periostin concentration of the control group, $p < 0.001$.

3.2.3.2. Periostin concentration in disease group

Table 3.19. *Periostin concentrations in disease groups according to history of heart failure*

Periostin (ng/mL) in disease group			**M ± SD**	**p value ***
First time	History of heart failure	Yes (n = 45)	237,80 ± 89,22	**< 0,001**
		No (n = 108)	150,29 ± 61,75	
Second time	History of heart failure	Yes (n = 45)	98,03 ± 35,20	**0,001**
		No (n = 108)	76,00 ± 30,38	

Acute MI patients with a history of heart failure had significantly higher periostin levels than those without a history of heart failure at both testing times: upon admission and 3 months after acute MI.

Table 3.20. *Periostin concentrations in the PCI and non-PCI groups*

Periostin (ng/mL)			**Trung vị**	**KTPV**	**p**
First time	PCI	Yes	127,33	113,11 - 156,55	**< 0,001**
		No	177,19	125,51 – 219,08	
Second time	Non-PCI	Yes	67,91	50,47 - 79,08	**< 0,001**
		No	86,52	70,11 - 113,61	

Periostin in the PCI group was lower than that in the non-PCI during hospitalization and 3 months after AMI, $p < 0.001$.

3.2.3.3. Differences of admission periostin in echocardiographic parameters 3 months after AMI

Table 3.23. *Differences of admission periostin in LVEF parameters on echocardiography 3 months after AMI*

Parameters	**Grouping**	**n**	**Periostin (ng/mL)**		**p value**
			Median	**Interquartile range**	
LVEF (%)	≥ 50	69	127,30	113,72 – 150,76	**< 0,001**
	< 50	84	201,22	132,36 – 245,58	

Periostin concentration in LVEF ≥ 50% group < remaining group, $p < 0.001$.

3.3. THE RELATIONSHIP BETWEEN SERUM PERISTIN CONCENTRATIONS WITH NT-PROBNP, LVEF, GRACE SCORE, MESA SCORE AND THE PREDICTIVE VALUE OF SERUM PERIOSTIN CONCENTRATION AFTER AMI

3.3.1. Correlation between periostin and parameters related to myocardial remodeling on echocardiography 3 months after AMI

Table 3.29. *Correlation between periostin and LVEF on echocardiography 3 months after AMI*

Echocardiography after AMI 3 months	**Periostin (ng/mL) at hospitalization**	
	r*	**p**
LVEF (%)	- 0,471	**< 0,001**

There was a negative correlation between periostin and LVEF after acute MI 3 months, $p < 0.05$. **LVEF after 3 months of acute MI = 62.044 - 0.072 x periostin concentration.**

3.3.2. The correlation between periostin and NT-proBNP at admission and 3 months after MI in AMI patients

Table 3.30. *Correlation between admission periostin and NT-proBNP*

NT-proBNP (pg/mL)	**Periostin (ng/ mL)**	
	r	**p**
At admission	0,411	**< 0,001**
After AMI 3 months	0,446	**< 0,001**

There was a strong positive correlation between periostin at admission and NT-proBNP at admission and NT-proBNP after 3 months ($p < 0.05$).

3.3.3. Correlation between admission periostin and cardiovascular risk prognostic factors

Table 3.31. *Correlation between admission periostin and cardiovascular risk prognostic factors*

Factors	Periostin (ng/ mL) at admission	
	r*	**Giá trị p**
Killip score	0,267	**0,001**
GRACE score	0,521	**< 0,001**
MESA score	0,390	**< 0,001**
Gensini score *	0,057	0,674
SYNTAX I score *	0,119	0,377
SYNTAX II – PCI score *	0,118	0,380
SYNTAX II – CABG score *	0,019	0,888
PCI *	- 0,311	**< 0,001**

Periostin correlated positively with Killip, GRACE and MESA scores, and negatively correlated with PCI intervention, $p < 0.001$. MESA score = 12.323 + 0.023 x periostin concentration.

3.3.4. Prognostic value of cardiac function of periostin in patients after AMI

Table 3.35. *Sensitivity and specificity of periostin in predicting heart failure in AMI patients (n = 153)*

Parameter	**AUC**	**Cut-off point**	**Se (%)**	**Sp (%)**	**PPV (%)**	**NPV (%)**	**P value**
Periostin	0,763	183,89	58,33	95,65	13,42	0,44	**< 0,001**

If peristin concentration at admission ≥ 183.89 ng/mL, the prediction of LVEF < 50% has an area under the ROC curve of 0.763 with a specificity of 95.65%.

3.3.5. Prediction of risk of LVEF < 50% 3 months after MI based on periostin cut-off point

Table 3.37. *Prediction of LVEF risk < 50% based on periostin cut-off point*

Periostin (ng/mL)	LVEF (n)		OR
	< 50%	≥ 50%	
Increasing (≥ 183,89)	49	4	OR = 22,75, p < 0,001, 95% CI = 7,58 - 68,27
Non-increasing (< 183,89)	35	65	

If peristin concentration at admission is ≥183.89 ng/ml, the predicted risk of LVEF below 50% will be 22.75 times greater than the remaining group.

3.3.6. Multivariate logistic regression model predicts low LVEF after 3 months

Table 3.39. *Multivariate logistic regression model predicting heart failure after 3 months according to periostin, NT-proBNP, GRACE score, MESA score*

Parameters	OR adjusted	95% CI	p value
Periostin	1,024	1,012 – 1,036	**< 0,001**
NT-proBNP	1,000	1,000 – 1,001	**0,008**

In the multivariate logistic regression model predicting the risk of low LVEF 3 months after AMI, the concentrations of periostin and NT-proBNP at admission were statistically significant (p < 0.05), with each unit increase in periostin concentration increasing the risk of heart failure 1.024 times.

3.3.7. Combined value of periostin and NT-proBNP in predicting the risk of low LVEF 3 months after AMI

Table 3.41. *Prediction of low LVEF risk based on the combination of periostin and NT-proBNP concentrations in AMI patients*

Combination	OR	p	Se (%)	Sp (%)	PPV (%)	NPV (%)
Periostin (+) and NT-proBNP (+)	44,00	< **0,001**	39,85	98,55	97,06	57,14
Periostin (+) and NT-proBNP (-)	5,18	**0,006**	19,65	95,65	84,21	49,25
Periostin (-) and NT-proBNP (+)	1,92	0,206	15,48	91,30	68,42	47,01
Periostin (-) and NT-proBNP (-)	0,06	< **0,001**	26,19	14,49	27,16	13,89

If periostin increases and NT-proBNP increases, the predicted risk of low LVEF is 44 times higher than in the remaining group of patients, $p < 0.001$.

Chapter 4
DISCUSSION

4.1. GENERAL CHARACTERISTICS OF THE STUDY SAMPLE

4.1.1. Demographics

Age: The risk of cardiovascular diseases increases with age. In our study, up to 81% of AMI patients were 60 years old or older. The average age of the group was 70.29 ± 12.32, the youngest patient was 38 years old and the oldest was 96 years old.

Gender: Men are at higher risk of cardiovascular diseases than women, according to the MESA score calculation, male gender is a factor that increases the cardiovascular risk score [37]. The results of this study showed that the number of men is higher than that of women, the male/female ratio = 1.50.

BMI: Older people are limited in physical activity in health training to control weight well, which leads to a state of being easily overweight and obese. Up to 42.48% of AMI patients were obese.

4.1.2. Pre-historical characteristics

Hypertension and diabetes will affect the prognosis of patients after AMI. The proportion of patients with a history of hypertension in this study is large, up to 62.75% (*Table 3.2*). This is a modifiable risk factor, commonly found in cardiovascular disease and death in the elderly [21].

4.1.3. Risk stratification according to cardiovascular risk scores

GRACE score: The average score was quite high: 126.83 ± 27.08 points, the high-risk group accounted for more than half (52.29%) (*Table 3.4*), thereby showing that the patient group in the study was generally prone to cardiovascular events after discharge.

MESA score: Patients in the very high-risk subgroup accounted for the majority with 62.74%. The high MESA score in both the STCL and KSTCL NMCT groups was consistent with the fact that the majority of patients were elderly, had many cardiovascular risk factors, and had other associated diseases.

Gensini and SYNTAX scores: The average Gensini score was 32.46 ± 23.60 points, while the SYNTAX I and SYNTAX II scores were at the medium-high level (*Table 3.11*). This is also quite similar to the assessment by GRACE scale that these subjects are generally susceptible to cardiovascular events after discharge from the hospital.

4.2. CLINICAL, PARACLINICAL CHARACTERISTICS AND SERUM PERIOSTIN CONCENTRATION IN AMI PATIENTS

4.2.1. Clinical characteristics

Chest pain upon admission: **96.08% had chest pain and the p**roportion of patients without chest pain accounted for 3.92% (*Table 3.5*). The majority of patients were hospitalized for angina, accounting for 87.58% and typical angina accounted for the majority with 84.97% of chest pain cases.

Killip classification: When patients are admitted to the hospital, it is necessary to quickly assess the severity of acute heart failure to stratify risk and predict prognosis. The majority of patients in our study group had Killip classification when they first entered the treatment department as Killip I (60.78%), while cardiogenic shock accounted for only 5.23% (*Figure 3.2*).

Clinical abnormalities at admission: Nearly half of the patients had high blood pressure at admission (49.67%). Among the cases of high blood pressure at admission, stage II and III hypertension accounted for half of the cases (*Table 3.7*), indicating the need to increase the rate of stricter blood pressure control in patients.

4.2.2. Paraclinical features

Laboratory characteristics of AMI patients: Cardiac enzymes are elevated and change rapidly over time, so repeated testing is needed to determine peak troponin concentrations, which is the basis for risk stratification for AMI patients [2]. Hs-Troponin T increased significantly in this study, in which hs-Troponin T in the ST elevation AMI group was much higher than in other (*Table 3.9*).

Blood NT-proBNP: is a commonly used paraclinical test for AMI patients for the purpose of diagnosing and predicting heart failure [3]. Non-ST-elevation AMI patients have less dramatic clinical manifestations than those with ST-elevation AMI. If NT-proBNP concentration is < 300 pg/mL, the diagnosis of acute heart failure is excluded [10]. NT-proBNP concentration in the study group far exceeded this threshold, indicating that many people in the group are likely to have acute heart failure.

ECG: when a patient has clinically suspected signs of AMI, ECG is the first choice to rely on changes on the electrocardiogram to guide the diagnosis. In this study, 48.33% of cases had arrhythmia (*Table 3.10*). We noted on ECG that most of the lesions were in the anterior wall.

Coronary angiography lesions: the anterior interventricular artery predominates with 92.98% of coronary lesions, the circumflex artery accounts for 50.88% and the right coronary artery accounts for 54.39% (*Table 3.11*). With stenosis ≥ 90%, the anterior interventricular artery accounts for the largest number. In terms of the number of coronary branches damaged, 1 branch accounts for 24.56%, 2 branches account for 50.88% and 3 branches account for 24.56%.

Echocardiography during hospitalization: 66.01% had regional wall motion disorders. There was a difference in LVEF in each subgroup of the 2 groups of AMI patients. LVEF in the ST-elevation AMI group was lower than in the non-ST-elevation group and the rate of preserved LVEF in the ST-elevation group was 36.36% while in the non-ST-elevation group it was 73.47%, consistent with the nature of myocardial damage in the 2 groups of and ST-elevation AMI and non-ST-elevation. The majority of subjects with a history of heart failure who developed acute MI in this study had preserved or mildly reduced LVEF.

Echocardiography 3 months after MI: LVEF in the ST-elevation group was significantly lower than LVEF in the non-ST-elevation group (*Table 3.14*), while echocardiography during hospitalization did not show this difference. This may be explained by the fact that the cardiac remodeling process after acute MI requires a long time to replace dead myocardial tissue due to infarction with non-functional fibrotic scar tissue, thereby causing a greater decrease in LVEF in the more severe group - the ST-elevation AMI group.

4.2.3. Serum periostin concentrations in AMI patients

Periostin concentrations in the patient and control groups: the periostin concentration in AMI patients tested the first time reached the highest threshold (*Table 3.17*). The second test after 3 months of A MI showed that the periostin concentration decreased, while the periostin concentration in the control group was the lowest. This

significant difference in periostin concentration is completely consistent with the pathophysiological progression of changes in periostin concentration over time when the heart is damaged [160].

The periostin concentration in non-PCI group was significantly higher than PCI group (*Table 3.20*). This result shows that the effectiveness of coronary intervention by PCI will improve the subsequent prognosis in patients with acute MI compared with patients who did not undergo PCI. In addition, the periostin concentration in the Killip I group was lower than in the Killip II-IV group, suggesting that periostin is more likely to correlate with the severity of the disease.

The difference of periostin in echocardiographic parameters after AMI 3 months: After the patient has an AMI, periostin stimulates myocardial remodeling excessively, leading to a state of non-function fibrotic scar tissue to replace the damaged myocardial area, which will reduce heart function, reduce LVEF, reduce cardiac contractility and lead to expansion of the size of the heart chamber. The more periostin is produced, the more obvious the remodeling process becomes. The concentration of periostin in the LVEF ≥ 50% group is much lower than that in the remaining group (*Table 3.23*).

Relationship between admission periostin concentration and NT-proBNP: High NT-proBNP concentration often signals a poor prognosis for patients with heart failure. The periostin concentration in the high NT-proBNP group at admission (≥ 125 pg/mL) higher than the periostin concentration in the remaining groups (*Table 3.24*). This shows that periostin concentration is related to the severity of heart failure.

The relationship between periostin concentration at admission and the GRACE score: Periostin concentration in the high-risk group

in the GRACE score was higher than that in the remaining group (*Table 3.25*). This further confirms that periostin is related to the severity of the disease, and can be selected for use as a biomarker to predict the degree of heart damage (more specifically, the prognosis of heart function) after AMI.

Correlation between periostin concentration at admission and MESA heart failure risk assessment score: Serum periostin concentration in the high to very high risk group in the MESA score was significantly higher than that in the low and intermediate risk MESA score groups, $p < 0.001$. This helps confirm that periostin concentration is correlated with MESA score, which also means that periostin is more likely to be a biomarker in predicting the risk of heart failure after AMI.

4.3. THE RELATIONSHIP BETWEEN SERUM PERISTIN CONCENTRATIONS WITH NT-PROBNP, LVEF, GRACE SCORE, MESA SCORE AND THE PREDICTIVE VALUE OF SERUM PERIOSTIN CONCENTRATIONS FOR CARDIAC SYSTOLIC FUNCTION IN PATIENTS AFTER ACUTE MI

4.3.1. Correlation between periostin and some parameters

Correlation between periostin at admission and LVEF on echocardiography 3 months after MI: periostin concentration is positively correlated with LVEDD, and negatively correlated with LVEF 3 months after MI, these correlations are statistically significant with $p < 0.05$ (*Table 3.29*). This means that the higher periostin concentration, the higher the possibility of heart failure 3 months after AMI, shown through the correlation equations

(*Figure 3.7*): **LVEF 3 months after AMI = 62.044 - 0.072 x periostin concentration.**

Correlation between serum periostin concentration at admission and NT-proBNP: there was a strong positive correlation between

periostin concentration at admission and NT-proBNP at admission and 3 months after AMI (*Table 3.30*), indicating that periostin concentration is a factor capable of predicting cardiac function 3 months after AMI.

Correlation between periostin during hospitalization and cardiovascular risk prognostic scores: Periostin concentration is positively correlated with Killip score (*Table 3.31*). This result further confirms the ability of periostin to predict the severity of acute MI patients. In addition, there is a strong positive correlation between serum periostin concentration and GRACE score, meaning that the higher the periostin concentration, the more likely the patient is to have heart failure 3 months after AMI, as shown by the linear regression equation (*Figure 3.6*): **MESA score = 12.323 + 0.023 x periostin concentration**.

There is an inverse correlation between periostin concentration and PCI treatment. With the great effects that revascularization treatment brings, choosing PCI for AMI patients is considered the foundation of current treatment methods.

4.3.2. Prognostic value of cardiac systolic function of periostin in patients after AMI

The sensitivity and specificity of periostin during hospitalization in the prognosis of low LVEF in AMI patients: The best cut-off point in the prognosis of low LVEF of periostin concentration was ≥ 183.89 ng/mL, with a sensitivity of 58.33% and a specificity of 95.65%, AUC ROC was 0.763, $p < 0.001$ (*Table 3.35*). The prognostic value was quite good with high specificity.

The prediction of low LVEF risk 3 months after AMI based on the cut-off point of periostin: In the univariate logistic regression model, periostin and the MESA score were significant in predicting the risk of low LVEF in AMI patients. After adjustment in the

multivariate logistic regression model, the periostin group ≥ 183.89 ng/mL was 22.75 times more likely to have low LVEF than the other group with $p < 0.05$ (*Table 3.37*).

The multivariate logistic regression model predicting low LVEF 3 months after MI: The model predicts the probability of low LVEF 3 months after MI based on 4 variables: MESA, GRACE scores, NT-proBNP and periostin (*Figure 3.13*). In the multivariate logistic regression model predicting the risk of heart failure 3 months after MI, each unit increase in periostin concentration increases the risk of heart failure 1.024 times (*Table 3.39*). Multivariate regression analysis results showed that periostin is an independent prognostic factor predicting heart failure 3 months after MI.

Combined value of periostin during hospitalization and NT-proBNP in predicting the risk of low LVEF 3 months after AMI: If the periostin concentration ≥ 183.89 ng/mL and NT-proBNP ≥ 1,564.00 pg/mL, the probability of patients with low LVEF 3 months after AMI is predicted to be 44 times higher than the remaining group of patients, with $p < 0.001$ (*Table 3.41*). This combination has a very high specificity (98.55%), but a low sensitivity (39.85%). In addition, the positive predictive value of this combination is also very high (97.06%) but the negative predictive value is low (57.14%).

The combination of periostin at admission and NT-proBNP improved the predictive value of heart failure risk 3 months after AMI, with the AUC ROC of this combination being greater than that of periostin alone (0.771 vs. 0.763). Compared with periostin alone, this combination improved specificity from 95.65% to 98.55%.

CONCLUSIONS

Through the study of serum periostin concentrations in 153 myocardial infarction patients and 153 healthy subjects from September 2019 to March 2023, we achieved the following conclusions:

1. Clinical, paraclinical characteristics and serum periostin concentration in acute myocardial infarction patients

- In AMI patient group, the majority had Killip I (60.78%). There were 3.92% of AMI patient without chest pain and the regional movement disorder on echocardiography was quite high (66.01%).

- The median serum periostin concentration in normal people was 63.04 ng/mL (40.96 - 80.98 ng/mL), increasing when the patient had AMI, peaking at 5 - 7 days after AMI with a median of 149.37 ng/mL, then gradually decreasing over time.

- The periostin concentration varied according to the Killip classification: low in patients with Killip I, if Killip was higher, the periostin was also higher.

- The LVEF $\geq$ 50% and normal LVEDD group had lower periostin concentration than the remaining group.

- Periostin concentration changed according to NT-proBNP level at admission: patients in the NT-proBNP group $\geq$ 125 ng/mL had higher periostin concentration than those in the NT-proBNP group < 125 ng/mL.

- Periostin concentration was low in the group with low or intermediate GRACE, MESA risk stratification, periostin was higher in the GRACE, MESA high or very high risk group. At the same time, periostin concentration was low in the PCI group and higher in the non-PCI group.

2. The relationship between serum periostin concentration with NT-proBNP, LVEF, GRACE score, MESA heart failure prediction score and the predictive value of cardiac systolic function of periostin in patients after AMI:

- Serum periostin concentration was strongly inversely correlated with LVEF 3 months after AMI; strongly positively correlated with NT-proBNP both at admission and 3 months after acute MI ($p < 0.001$). Periostin had a strong positive correlation with GRACE and MESA scores. MESA score = 12.323 + 0.023 x periostin concentration.

- The cut-off point of serum periostin concentration in AMI patients was 183.89 ng/mL. The AUC ROC, sensitivity and specificity of periostin were 0.763, 58.33% and 96.65%, respectively, indicating that periostin's ability to predict cardiac function was better than NT-proBNP, GRACE score or MESA score.

- If the patient's periostin concentration is 183.89 ng/mL or higher, the risk of heart failure after 3 months can be predicted to be 22.75 times higher than when the patient's periostin concentration is less than 183.89 ng/mL. LVEF 3 months after AMI = 62.044 - 0.072 x periostin concentration.

- Patients with serum periostin levels of 183.89 ng/mL or higher and NT-proBNP levels of 1,564.00 pg/mL or higher are 44 times more likely to have low LVEF than the other group.

RECOMMENDATIONS

- Serum periostin can be used to predict cardiac systolic function in patients after AMI to stratify risk, thereby optimizing appropriate treatment and monitoring plans.

- Periostin and NT-proBNP can be used in combination during hospitalization to predict cardiac function in patients after acute MI to increase specificity and prognostic efficiency.

THESIS-RELATED PUBLICATIONS

1. Nguyen Trung Tin, Doan Chi Thang, Huynh Van Minh, "Periostin, a new marker in the prognosis of cardiac function after acute myocardial infarction", Journal of Vietnamese Cardiology, volume 98, October 2021.
2. Nguyen Trung Tin, Doan Chi Thang, Huynh Van Minh, Phan Thi Minh Phuong, "Preliminary results of periostin alterations in patients after non-ST elevation myocardial infarction", Hue Journal of Medicine and Pharmacity, volume 13(7), December 2023.
3. Nguyen Trung Tin, Huynh Van Minh, Doan Chi Thang, Phan Thi Minh Phuong, "Serum periostin levels in acute myocardial infarction patients: A 3-month follow-up study", ACTA INFORM MED, volume 31(3), June 2023.