

## Assessment of and N-Terminal B-Type Natriuretic Peptide and cystatin-C of serum levels in patients with Heart Failure

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**Abstract: Background:** Heart failure timely and effective diagnosis and treatment directly affects the prognosis of patients, so early diagnosis of heart failure treatment is very important. The current diagnosis of heart failure has yet to be further improved. To investigate the relationship between plasma levels of cystatin-C and NT-proBNP in cardiac structure and function in patients with heart failure (HF) and the early detection of failure. **Methods:** Patients were recruited from the coronary care unit (CCU) of Al-Yarmouk Teaching Hospital and were admitted and verified as cases of HF by specialist cardiologists. Between the 1st of November 2017 and the 1st of April 2018; 48 patients (29 males and 19 females), were diagnosed to have HF and were included in the study. The total number of HF patients admitted to the CCU of the hospital during the study period was 100 patients but 52 patients were ruled out according to the exclusion criteria of the study such as Acute Myocardial Infarction, active myocarditis, Drug abuse or an alcohol drinker, renal failure. Apparently healthy subjects were recruited from the staff of Al-Mustansiriyah Medicine College. They comprised (40) subjects (30 males and 10 females). Each subject who was recruited in the control group has underwent a full history and physical examination with a recording of : age, gender, smoking, chronic diseases and medications. Any subject in control group must be fasting for 8-14 hours at the time of drawing of blood specimen. Consent was taken from all subjects in the control group after being told about the aim of the study. The plasma Galectin-3 and cystatin-C and NT-proBNP levels were compared between the two groups to observe the value of plasma Galectin-3 and cystatin-C combined with NT-proBNP in the diagnosis of heart failure. **Results:** the levels of plasma cystatin-C and NT-proBNP were significantly higher in patients with heart failure Compared with the healthy control group. The levels of plasma cystatin-C and NT-proBNP increased significantly ( $P < 0.01$ ). The area under the ROC curve for the combined detection of plasma cystatin-C and NT-proBNP was greater than the area under the NT-proBNP alone tests. **Conclusion:** The combined detection of cystatin-C and NT-proBNP has high sensitivity and specificity in the diagnosis of heart failure and can be used as a new detection mode.

**Keywords:** N-Terminal B-Type Natriuretic Peptide, cystatin-C.

## INTRODUCTION

Heart failure is a clinical syndrome that results when the heart is unable to provide sufficient blood flow to meet metabolic requirements or accommodate systemic venous return its timely and effective diagnosis and treatment directly affects the prognosis of patients (Brar, S. *et al.*, 2013), so early diagnosis of heart failure treatment is very important. This study was to investigate the relationship between plasma levels of cystatin-C and NT-proBNP in cardiac structure and function in patients with heart failure (HF) early detection of failure. The clinical data of 48 patients with heart failure and normal healthy people 40 subjects. The purpose of this study was to analyze the clinical significance of combined detection of plasma cystatin-C and N-terminal B-type natriuretic peptide in the diagnosis of heart failure value. The study found that inflammation can aggravate myocardial injury, thereby worsening cardiac function, plays a very important role in ventricular remodeling (Kalogeropoulos, A. P. *et al.*, 2012). Most of the inflammatory cytokines have a negative inotropic effect, thereby reducing myocardial contractility and cardiac output, worsening cardiac function (de Boer, R. A. *et al.*, 2009; & Van Den Borne, S.W. *et al.*, 2010). In recent years, studies have shown: cystatin-C can cause cardiac hypertrophy caused by inflammatory stimuli, resulting in decreased myocardial compliance, and thus cardiac dysfunction (Lok, D. J. *et al.*, 2013; de Boer, R. A. *et al.*, 2013; Sato, S. *et al.*, 2002; & Salvagno, G. L. *et al.*, 2014). Cystatin C (CysC), a non-glycosylated 13 kDa protein, is sensitive in the detection of early kidney damage (Oremus, M. *et al.*, 2014), because its level may increase when GFR is 70 mL/min or less. CysC levels are reported to be significantly associated with components of metabolic syndrome or cardiovascular diseases in adults. Moreover, high CysC levels are associated with the incidence of major cardiovascular events, including all-cause death, myocardial infarction, cerebrovascular disease, and peripheral vascular disease (Vickery, S. *et al.*, 2005; & Woitas, R. P. *et al.*, 2013), especially in the elderly, and also in subjects without chronic kidney disease (Palazzuoli, A. *et al.*, 2010). Furthermore, it has been suggested that cystatin C concentrations are directly related to both inflammation and atherosclerosis. Nevertheless, the link between inflammation, atherogenesis, cardiovascular risk, and cystatin C is still poorly understood. This brief report discusses recent data, contrasting findings and possible mechanisms involved in this interaction.

## MATERIALS AND METHODS

### Research Objects and Groups

The study was carried out at the department of Chemistry and Biochemistry / College of Medicine/ Al Mustansiriyah University. Patients were recruited from the coronary care unit (CCU) of Al-Yarmouk Teaching Hospital and were admitted and verified as cases of HF by specialist cardiologists. Between the 1st of November 2017 and the 1st of April 2018; (29 males and 19 females), aged  $\geq 30$  years, and we selected 48 patients were diagnosed to have HF.

### Patients were interviewed using a questionnaire that included:

- Time of admission to CCU after onset of chest pain.
- Past medical history which involved history of coronary heart disease, hypertension and its duration, family history of HF, history of DM, intake of drugs such as statins, current smoking or not and history or current alcohol consumption.

The questionnaire also included recording of socio-demographic measures that involved: age, gender, residence, educational level, and marital status. Patients with Heart failure but have the following conditions were excluded in this study:

1. Acute Myocardial Infarction
2. Active myocarditis.
3. Stroke, skeletal muscle injury, or trauma.
4. Age is  $<30$  years.
5. Prior inclusion in the present study.
6. Valvular heart disease

Individuals were considered as smokers when they were current smokers or had smoked in the past 30 days. A never-smoker is a person who either had never smoked at all or smoked less than 100 cigarettes.

Apparently healthy subjects were recruited from the staff of Al-Mustansiriyah Medicine College. They comprised (40) subjects (30 males and 10 females). Each subject who was recruited in the control group has underwent a full history and physical examination with a recording of : age, gender, smoking state , chronic diseases and medications. They have no symptoms or

history of coronary heart disease. They were age and sex-matched to study patients ( $41.55 \pm 7$ ) and also comply to the criteria of exclusion in patients group. In addition, they underwent electrocardiographic screening to check for any ECG changes which might exist in spite of no clinical features of HF so as to be excluded from the study.

Any subject enrolled in control group must be fasting for 8-14 hours at the time of drawing of blood specimen. Consent was taken from all subjects in the control group after being told about the aim of the study.

### METHOD

Blood Collection Was Performed At 8.00 – 9.00 A.M. In The Fasting State, Collected Blood Was Transferred Into The Tube While Ensuring Flowing Down The Wall Of The Tube, Then Serum Was Btained And Divided Into Aliquots In Eppendorf Tubes And Stored At  $-20^{\circ}\text{C}$  Until Analysis. Determination Of Serum **Nt-Probnp and Cystatin C** Level By **Afias ,Is A Fluorescence Immunoassay (Fia) For The Quantitative Determination Of Nt-Probnp And Cystatin C In Human Serum, Boditech**.

### Statistical Methods

SPSS 22.0 software was used for statistical analysis. The t test was used to measure the data between the two groups. Chi-square test was used to count data. Logistic regression was used to analyze the risk factors for screening heart failure. The test level was 0.05. When  $P < 0.05$ , has statistical significance. The working curve (ROC curve) of subjects tested separately and jointly with cystatin c and NT-proBNP was established to calculate their specificity and sensitivity.

## RESULTS

### Comparison between Heart Failure Group and Control Group in Plasma Levels of cystatin c and NT-proBNP .

Heart failure group increased significantly compared with the control group, the difference was statistically significant ( $P < 0.01$ , Table 1). Plasma levels of cystatin c and NT-proBNP in HF group were significantly higher than those in control group ( $P < 0.01$ , Table 1)

**Table 1:** Heart failure group and control group heart function and plasma levels of Galectin-3 and cystatin c and NT-proBNP

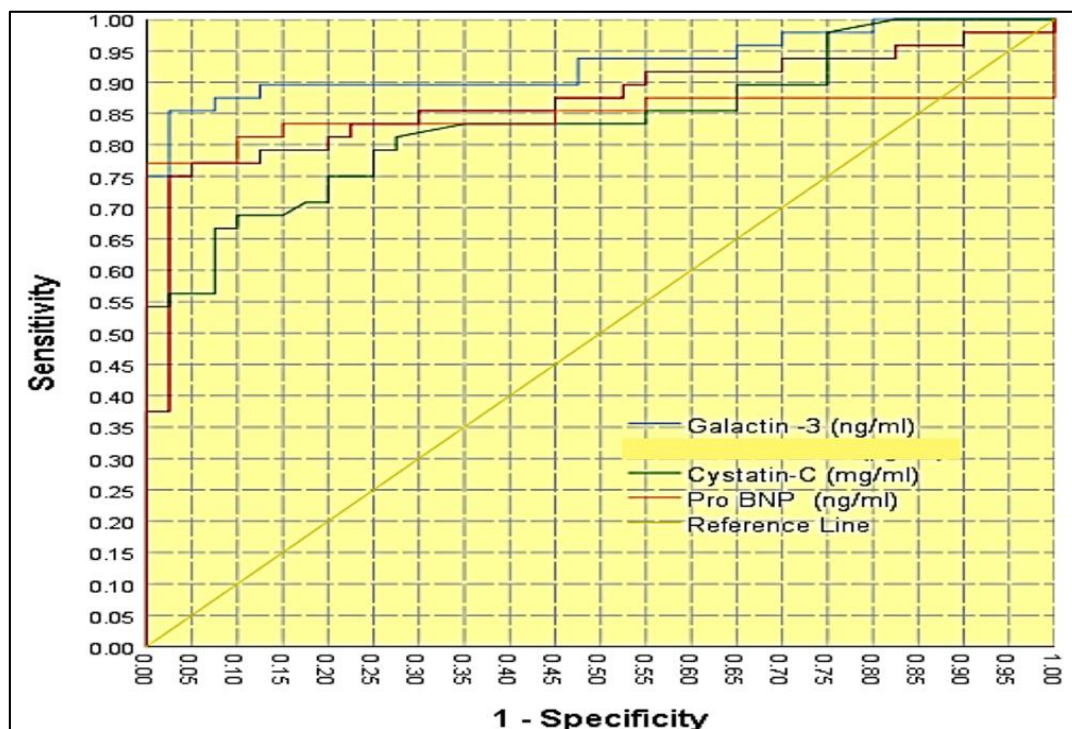
	Heart failure N= 48	Healthy controls N= 40	P value
<b>Cystatin-C (mg/ml)</b>	1.6220 $\pm$ 1.09337 (0.59-7.137)	0.69 $\pm$ 0.12 (0.52-1.01)	0.0001*
<b>NT-proBNP (ng/ml)</b> N-terminal pro b-type Natriuretic Peptide	763.1855 $\pm$ 298.94661 (22.1-2131.22)	134.54 $\pm$ 48.59 (59.30-232.10)	0.0001*

- Data were presented as Mean $\pm$ SD (Range)

\*Significant difference between two independent means using Students-t-test at 0.05 level.

**Table 2.** The Best Discriminative Area Under the Curve cystatin c and NT-proBNP Parameters that Best in HF.

Test Result Variable(s)	Cut-off value	Sensitivity	specificity	Area	P value
Cystatin-C (mg/ml)	0.77200	75.0	80	0.838	0.0001*
NT-proBNP (ng/ml)	195.40000	83.3	85	0.847	0.0001*

**Table 3:** correlation of plasma levels of cystatin c and NT-proBNP in HF group

		Correlations		
		Cystatin-C	NTPro BNP	Galactin -3
Cystatin-C	r	1	.397**	.016
	p		<b>0.005</b>	0.914
	N	48	48	48
NTPro BNP	r	.397**	1	.286*
	p	<b>0.005</b>		<b>0.049</b>
	N	48	48	48

\*\* . Correlation is significant at the 0.01 level (2-tailed).

\* . Correlation is significant at the 0.05 level (2-tailed).

## DISCUSSION

In clinical work, the diagnosis and differential diagnosis of heart failure is still a major problem, easily lead to missed diagnosis. Rapid progress of heart failure, once the condition deteriorated, often endanger the lives of patients. heart failure with poor prognosis (Yancy, C. W. *et al.*, 2017).

In recent years, NT-ProBNP has become hot spots in the early diagnosis of heart failure (Bao, J. *et al.*, 2016; Yancy, C. W. *et al.*, 2013; Oremus, M. *et al.*, 2014; Roberts, E. *et al.*, 2015; & Balion, C. *et al.*, 2014). This study aimed to explore the value of cystatin c and N-terminal B-type natriuretic peptide in the diagnosis of heart failure.

This study aimed to explore the value of cystatin-C and N-terminal B-type natriuretic peptide in the diagnosis of the heart failure. A large number of studies have shown that BNP can better reflect the function of the heart (Cardiovascular Diseases Section of Chinese Medical Association. 2014), making it widely used in the diagnosis of heart failure. BNP is a chemical that is pulled in the ventricular wall and released into the blood by cardiomyocytes (Simonini, M. *et al.*, 2015; & Palazzuoli, A. *et al.*, 2010). BNP is also present in normal tissues and is present in very low plasma concentrations. Cardiomyocytes release BNP while also releasing equimolar NT-ProBNP into the bloodstream. Compared with BNP, NT-ProBNP has higher stability in blood plasma, longer half-life and is less affected by other substances. As the heart expands, the hemodynamics and neuroendocrine activities in the heart cavity change. The higher the pressure in the ventricle, the stronger the ventricular wall is pulled and



the higher the level of NT-ProBNP secreted by cardiomyocytes (Sata, Y., & Krum, H. 2010). In the present study, the level of NT-proBNP was significantly higher than that of the control group, confirming that NT-proBNP has a very important clinical value in the diagnosis of heart failure. Nomura *et al.*, (2002) showed that serum NT-proBNP were elevated in heart failure and that agree with this study.

## CONCLUSION

In this study, our results showed that plasma levels of NT-proBNP and cystatin c in patients with heart failure were significantly higher than those in healthy controls, both of which could be used as indicators of heart failure. There was significant difference in the levels of NT-proBNP and cystatin c between the heart failure group, The level was significantly increased ( $P < 0.01$ ).

ROC curve results show that the detection of NT-proBNP and cystatin c alone in the diagnosis of acute heart failure has a good sensitivity and specificity.

NT-ProBNP is even better at heart failure with renal insufficiency. Therefore, when the two jointly examined, the sensitivity and specificity are significantly improved, there is an important clinical value.

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