

Predictive Effect of CA125 on Adverse Cardiovascular Events in Patients with Chronic Heart Failure

Yuqing Duan, Yuan Xu, Li Li, Jun Yin, Qing Huang, Hong Wang, Zicheng Mai, Xiaohu Ma*

Department of Cardiology, Shizuishan Second People's Hospital, Shizuishan, China

Email: dyqqh@126.com, *gsss0027@163.com

How to cite this paper: Duan, Y.Q., Xu, Y., Li, L., Yin, J., Huang, Q., Wang, H., Mai, Z.C. and Ma, X.H. (2024) Predictive Effect of CA125 on Adverse Cardiovascular Events in Patients with Chronic Heart Failure. *International Journal of Clinical Medicine*, 15, 382-388.

<https://doi.org/10.4236/ijcm.2024.158024>

Received: July 6, 2024

Accepted: August 13, 2024

Published: August 16, 2024

Copyright © 2024 by author(s) and Scientific Research Publishing Inc.
This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).

<http://creativecommons.org/licenses/by/4.0/>



Open Access

Abstract

Objective: To study the expression of CA125 in the serum of patients with CHF and the relationship between CA125 level and the occurrence of adverse cardiovascular events. **Methods:** The clinical data of 132 patients with CHF admitted to Shizuishan Second People's Hospital from January 2023 to December 2023 were collected and divided into heart function II group, heart function III group, heart function IV group according to cardiac function. 44 healthy subjects who underwent physical examination during the same period were selected as the control group. The clinical data of CA125, NT-proBNP, echocardiography and other clinical data of the four groups were compared, and the incidence of major adverse cardiovascular events was followed up for 12 months. **Results:** Compared with the control group, the CA125 level in the CHF group was significantly increased ($P < 0.05$). In CHF patients, CA125, NT-proBNP, and LVEDD levels were positively correlated with cardiac function grade, and LVEF was negatively correlated with cardiac function grade ($P < 0.05$). The mortality rate and re-hospitalization rate of the group with CA125 serum concentration greater than 35 U/ml were significantly increased ($P < 0.05$). **Conclusion:** Serum CA125 level is related to the cardiac function level in CHF patients and increases with the deterioration of cardiac function. The increase of the index is related to the mortality rate and re-hospitalization rate, suggesting that CA125 can be used as an indicator to reflect the severity of heart failure and prognosis monitoring.

Keywords

Chronic Heart Failure, CA125, NT-proBNP, Major Adverse Cardiovascular Events

1. Introduction

Chronic heart failure (CHF) is the terminal manifestation of all cardiovascular diseases and the main cause of death. It is an increasingly serious public health problem facing the clinic and society. The incidence of chronic heart failure in China has been increasing year by year. Currently, the number of people suffering from heart failure in my country has reached 8.9 million, and the number of deaths from cardiovascular diseases accounts for 45.5% of the total number of deaths [1].

B-type natriuretic peptide (BNP) is the most widely used biomarker of heart failure. It is related to the increase in ventricular pressure and load. Due to its limitations, its predictive effect on adverse cardiovascular events is unsatisfactory [2]. Antigen carbohydrate 125 (CA125) is highly expressed in ovarian and metastatic malignant tumors, it has been found to be associated with mechanical stress and inflammatory response caused by serous effusion, with a half-life of 4.8 days [3]. Studies have shown that CA125 is closely related to cardiac function and hemodynamic parameters, and plays an effective role in predicting adverse cardiovascular events [4]. Exploring the relationship between CA125, BNP and cardiac function can further enhance the prediction, treatment and prognosis of heart failure [5].

This study mainly analyzed the expression of CA125 in the serum of CHF patients, the relationship between CA125 levels and the occurrence of adverse cardiovascular events, and explained the role of CA125 in predicting adverse cardiovascular events in patients with chronic heart failure.

2. Materials and Methods

2.1. General Information

Clinical data of CHF patients admitted to our hospital from January 2023 to December 2023 were collected. 1) Inclusion criteria: The diagnostic criteria for heart failure refer to the fourth edition of Practical Cardiology edited by Chen Haozhu, using the modified Framingham heart failure diagnostic criteria, and the classification of heart failure uses the NYHA heart function classification standard of the New York Heart Association. 2) Exclusion criteria: Patients with acute coronary syndrome, acute infection, tuberculosis, tumors, severe liver and kidney diseases, and surgical trauma in the past three months.

A total of 132 CHF patients were included and divided into heart function II group (46 cases), heart function III group (42 cases), heart function IV group (44 cases) according to heart function. Another 44 healthy subjects who underwent physical examination during the same period were selected as the control group. The general information is no significant difference between the groups ($P > 0.05$), which was comparable (Table 1).

2.2. Method

The clinical baseline data of the patients were collected and fasting venous blood was collected to measure the levels of CA125, NT-proBNP, CA199, CEA, and

Table 1. Comparison of general clinical data among different groups.

	Control Group	NYHA II	NYHA III	NYHA IV
Quantity	44	46	42	44
Age	70.52 ± 8.92	69.13 ± 8.27	70.45 ± 9.33	69.25 ± 7.37
Gender (male/female)	20/24	24/22	21/21	21/23
Basic heart disease				
coronary heart disease		30	22	25
Hypertensive heart disease		4	6	4
Valvular heart disease		6	8	4
Dilated cardiomyopathy		0	4	5
Restrictive cardiomyopathy		0	2	3
Other		6	2	3
Treatment				
ACEI/ARB/ARNI		40/46 (87%)	35/42 (83%)	32/44 (73%)
MRA		40/46 (87%)	36/42 (86%)	40/44 (91%)
B-blocker		32/46 (70%)	36/42 (86%)	35/44 (80%)
SGLT-2inhibitor		30/46 (65%)	33/42 (79%)	39/44 (89%)
Diuretic		33/46 (72%)	40/42 (95%)	43/44 (98%)

AFP. Echocardiography was performed to measure LVEDD and LVEF. All CHF patients were discharged after receiving standardized drug treatment. After discharge, the two groups of patients were followed up for 12 months by telephone and outpatient visits to observe the incidence of major adverse cardiovascular events 12 months after treatment, with the main indicators being the rate of re-hospitalization and mortality.

Blood samples were collected from all patients or their families after informed consent, and the blood sample collection and experimental process were approved by the Medical Ethics Committee of Shizuishan Second People's Hospital.

2.3. Statistical Method

SPSS 23.0 was used for statistical analysis. The measurement data were expressed as (mean ± standard deviation). The t test was used for comparison between groups, and the variance test was used for comparison between multiple groups. The count data were expressed as [n (%)] and compared with the χ^2 test. The influencing factors were analyzed by multivariate logistic regression, and the test level was $\alpha = 0.05$.

3. Result

3.1. Comparison of Four Groups of CA125, CA199, CEA, AFP, LVEF, and LVEDD

Compared with the control group, the differences in CA125, NT-proBNP, LVEDD,

and LVEF in the CHF group were statistically significant ($P < 0.05$), and were related to the cardiac function level of CHF patients. Among them, LVEF was negatively correlated with the cardiac function grade, and CA125, BNP and LVEDD levels were positively correlated with cardiac function classification, and the results were statistically significant ($P < 0.05$). There was no significant difference in CA199, CEA, and AFP levels ($P > 0.05$) (**Table 2**).

Table 2. Comparison of four groups of CA125, CA199, CEA, AFP, LVEF, and LVEDD.

	Control Group	NYHA II	NYHA III	NYHA IV
NT-proBNP	188.11 ± 152.59	983.46 ± 934.31 ^a	4192.86 ± 1969.22 ^{ab}	10,212.92 ± 5721.89 ^{abc}
CA125	9.21 ± 2.64	16.96 ± 11.31 ^a	60.04 ± 80.91 ^{ab}	205.39 ± 171.15 ^{abc}
CA199	8.43 ± 3.89	8.12 ± 2.97	8 ± 3.09	8.59 ± 3.22
AFP	3.27 ± 1.04	3.54 ± 2.03	4.4 ± 4.25	3.52 ± 1.82
CEA	2.17 ± 1.24	2.09 ± 1.38	2.13 ± 1.2	2.55 ± 1.18
LVEDD	45.47 ± 2.49	49.62 ± 3.9 ^a	54.61 ± 6.53 ^{ab}	70.56 ± 6.83 ^{abc}
LVEF	67.45 ± 5.18	55.04 ± 10.87 ^a	48.69 ± 7.81 ^{ab}	40.07 ± 7.44 ^{abc}

Note: ^aRepresents a statistically significant difference compared to the control group, $P < 0.05$; ^bRepresents a statistically significant difference compared to the NYHA II group, $P < 0.05$; ^cRepresents a statistically significant difference compared to the NYHA III group, $P < 0.05$.

3.2. Analysis of CA125 Serum Level and Rehospitalization Rate and Mortality Rate of Patients

All subjects were followed up for 12 months, and a total of 8 deaths and 20 re-admissions were reported in the 132 patients. The patients were divided into two groups according to whether the serum CA125 concentration was greater than 35 U/ml. The mortality rate and readmission rate of the group with a serum concentration greater than 35 U/ml were significantly increased, with a statistically significant difference ($P < 0.05$), indicating that as the CA125 level increases, the readmission rate and mortality rate of CHF patients also increase (**Table 3**).

3.3. Correlation Analysis of CA125 with LVEDD, LVEF, NT proBNP

CA125 is positively correlated with NT proBNP ($P < 0.001$), positively correlated with LVEDD ($P < 0.001$), and negatively correlated with LVEF ($P < 0.001$) (**Figure 1**).

4. Discussion

CA125 is a membrane-associated mucin that is mainly synthesized in mesothelial cells and is often used for the detection, prognosis and recurrence monitoring of ovarian cancer [6]. In patients with heart failure, increased interstitial venous

Table 3. Analysis of CA125 serum level and rehospitalization rate and mortality rate of patients.

CA125 serum level	Total	Number of deaths	mortality rate	Number of readmissions	re-hospitalization rate
>35	67	8	8/67 (11.9%)*	20	20/67 (29.9%)#
≤35	65	0	0 (0%)	6	6/65 (9.2%)

Note: *Indicates that the mortality rate was statistically different from that of the group with serum CA125 concentration < 35 U/ml, $P < 0.05$; #Indicates that the readmission rate was statistically different from that of the group with serum CA125 concentration < 35 U/ml, $P < 0.05$.

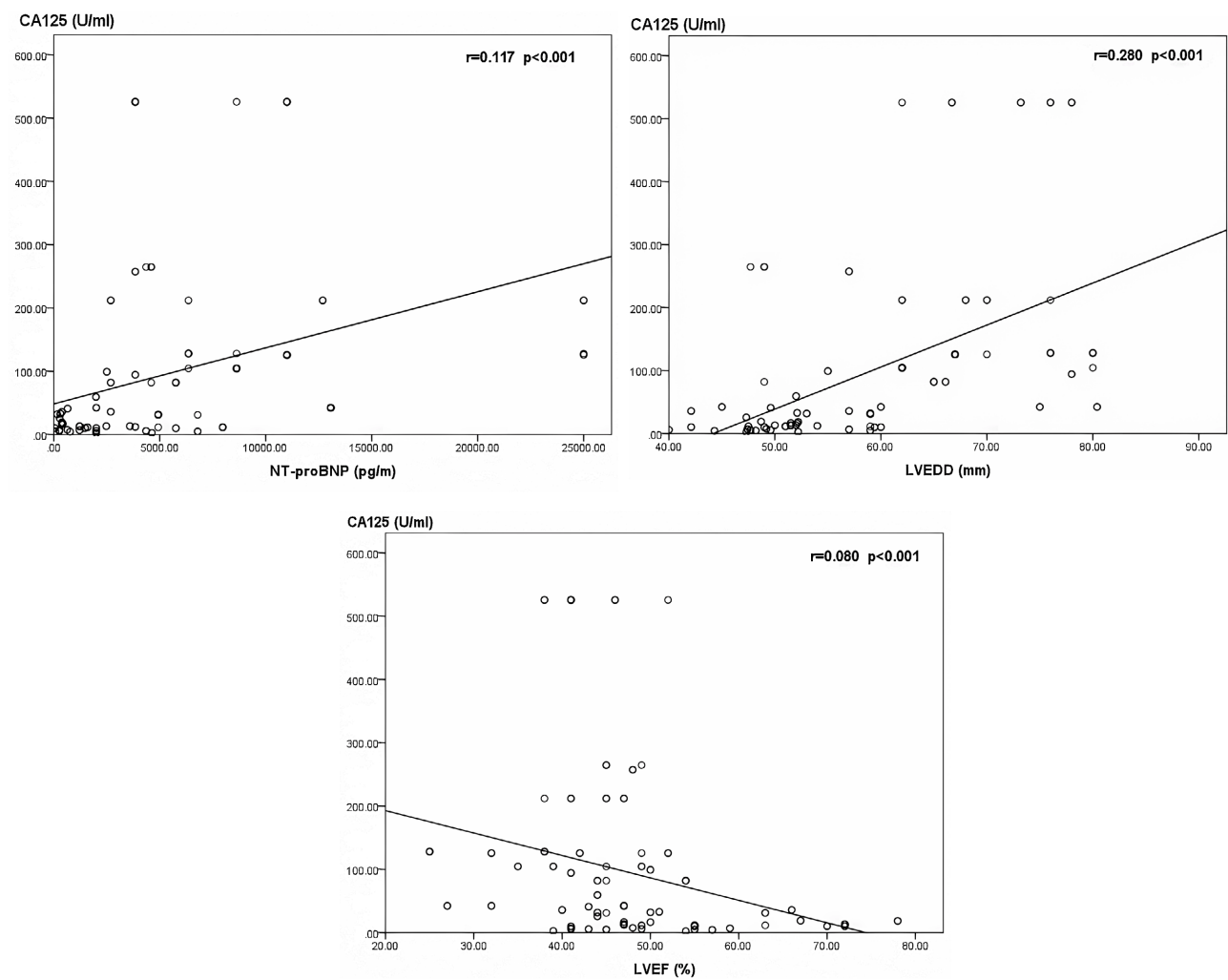


Figure 1. Correlation analysis of CA125 with LVEDD, LVEF, NT proBNP.

pressure and inflammatory stimulation cause mesothelial cell damage, which promotes the synthesis of CA125 in the pleural cavity. At the same time, macrophages are activated, which promotes the binding of CA125 to galectin 3 (Gal-3) pentamer, and acts on the fibroblast membrane through Gal-3 ligand, further leading to increased myocardial fibrosis and cardiac remodeling through

inflammatory and fibrotic pathways [4] [7] [8]. In recent years, the inflammatory response associated with heart failure has gradually received attention [2]. It has been found that the levels of multiple inflammatory factors in the serum of CHF patients are increased [9]. Among them, the inflammatory factors IL-1 β and TNF- α can promote the secretion of CA125. It is currently believed that CA125 is related to myocardial mechanical pressure and inflammatory factors in heart failure [10] [11].

Our study showed that serum CA125 was associated with the severity of heart failure. As heart failure worsened and cardiac function declined, the serum CA125 level increased, which was consistent with previous studies [12] [13], suggesting that CA125 can be used as an indicator to reflect the severity of heart failure.

Nunez *et al.* found that in AHF patients, CA125 was an independent predictor of mortality at 6 months, and high CA125 levels may be associated with increased all-cause mortality and re-hospitalization for heart failure [4]. This study followed up the patients for 12 months, and the results showed that CHF patients with CA125 > 35 U/ml had a higher mortality rate (11.9%) and re-hospitalization rate (29.9%). This suggests that CA125 can be used as a prognostic monitoring indicator for CHF patients.

5. Conclusion

The results of this study showed that serum CA125 levels are related to the cardiac function level of patients with chronic heart failure, and increase with the worsening of cardiac function. It can be used as an indicator of the severity of heart failure. It is not related to the cause of CHF, and is positively correlated with NT-proBNP and LVEDD, and negatively correlated with LVEF. In the study of prognosis, although our results show the important role of CA125 in the diagnosis and treatment of heart failure and prognosis, a larger sample size and longer follow-up time are still needed to verify the results so that they are more reliable.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

- [1] China Cardiovascular Health and Disease Report Editorial Group (2022) Summary of China Cardiovascular Health and Disease Report 2021.
- [2] Núñez-Marín, G., de la Espriella, R., Santas, E., Lorenzo, M., Miñana, G., Núñez, E., et al. (2021) CA125 but Not Nt-Probnp Predicts the Presence of a Congestive Intrarenal Venous Flow in Patients with Acute Heart Failure. *European Heart Journal. Acute Cardiovascular Care*, **10**, 475-483. <https://doi.org/10.1093/ehjacc/zuab022>
- [3] Núñez, J., de la Espriella, R., Miñana, G., Santas, E., Llacer, P., Núñez, E., et al. (2021) Antigen Carbohydrate 125 as a Biomarker in Heart Failure: A Narrative Re-

- view. *European Journal of Heart Failure*, **23**, 1445-1457.
<https://doi.org/10.1002/ehhf.2295>
- [4] Núñez, J., Bayés-Genís, A., *et al.* (2020) Clinical Role of CA-125 in Worsening Heart Failure: A BIOSTAT-CHF Study Subanalysis. *JACC: Heart Fail*, **8**, 386-397.
<https://doi.org/10.1016/j.jchf.2019.12.005>
- [5] Faggiano, P., D'Aloia, A., *et al.* (2006) Tumour Markers in Chronic Heart Failure. Review of the Literature and Clinical Implications. *Journal of Cardiovascular Medicine*, **7**, 573-579. <https://doi.org/10.2459/01.JCM.0000237903.95882.06>
- [6] Zhang, M., Zhang, Y., Fu, J. and Zhang, L. (2019) Serum CA125 Levels Are Decreased in Rectal Cancer but Increased in Fibrosis-Associated Diseases and in Most Types of Cancers. *Progress in Molecular Biology and Translational Science*, **162**, 241-252. <https://doi.org/10.1016/bs.pmbts.2018.12.012>
- [7] Murphy, S.P., Kakkar, R., McCarthy, C.P. and Januzzi, J.L. (2020) Inflammation in Heart Failure. *Journal of the American College of Cardiology*, **75**, 1324-1340.
<https://doi.org/10.1016/j.jacc.2020.01.014>
- [8] Crespo-Leiro, M.G. and Barge-Caballero, E. (2021) Advanced Heart Failure. *Heart Failure Clinics*, **17**, 533-545. <https://doi.org/10.1016/j.hfc.2021.06.002>
- [9] Adamo, L., Rocha-Resende, C., Prabhu, S.D. and Mann, D.L. (2020) Reappraising the Role of Inflammation in Heart Failure. *Nature Reviews Cardiology*, **17**, 269-285.
<https://doi.org/10.1038/s41569-019-0315-x>
- [10] Miñana, G., de la Espriella, R., Mollar, A., Santas, E., Núñez, E., Valero, E., *et al.* (2020) Factors Associated with Plasma Antigen Carbohydrate 125 and Amino-Terminal Pro-B-Type Natriuretic Peptide Concentrations in Acute Heart Failure. *European Heart Journal: Acute Cardiovascular Care*, **9**, 437-447.
<https://doi.org/10.1177/2048872620908033>
- [11] Llàcer, P., Gallardo, M.Á., *et al.* (2020) Comparison between CA125 and NT-proBNP for Evaluating Congestion in Acute Heart Failure. *Medicina Clínica*, **156**, 589-594. <https://doi.org/10.1016/j.medcli.2020.05.063>
- [12] Marinescu, M.C., Oprea, V.D., *et al.* (2024) Carbohydrate Antigen 125 (CA125): A Novel Biomarker in Acute Heart Failure. *Diagnostics*, **14**, Article 795.
<https://doi.org/10.3390/diagnostics14080795>
- [13] Llàcer, P., Bayés-Genís, A. and Núñez, J. (2018) Carbohydrate Antigen 125 in Heart Failure. A New Era in the Monitoring and Control of Treatment. *Medicina Clínica*, **152**, 266-273. <https://doi.org/10.1016/j.medcle.2019.01.015>