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Carbohydrate Antigen 125: An Predictor In Fluid Overload And In-Hospital Outcomes Of Heart Failure Patients

Phan Thai Hao[1], Huynh Van Toan[2]

[1]Department of Internal Medicine, Faculty of Medicine, Pham Ngoc Thach University of Medicine, Ho Chi Minh city, Vietnam
[2]Department of Internal Medicine, Binh Chanh General Hospital, Ho Chi Minh city, Vietnam

ABSTRACT

Background: Congestion is the main mechanism leading to disease progression and an important therapeutic target in heart failure (HF). Therefore, early detection of fluid overload in HF patients is essential. In recent years, increasing evidence has supported the use of carbohydrate antigen 125 (CA125) in cardiovascular diseases, particularly HF, with many studies worldwide demonstrating an association between CA125 levels and the degree of fluid overload. Before CA125, several prognostic biomarkers such as natriuretic peptides, high-sensitivity troponin, proadrenomedullin, soluble ST2, and galectin-3 had been evaluated. Despite the effectiveness of some prognostic markers, it remains challenging to identify predictors that can provide reliable prognostic information within a short timeframe for patients with acute heart failure (AHF). **Methods**: A prospective cohort study was conducted on 122 patients with heart failure who were hospitalized and treated at the Department of General Internal Medicine, Binh Chanh General Hospital, from March 2025 to September 2025. **Results**: There were 90 cases (74.6%) with fluid overload. The mean age was 68.1 ± 13.5 years, and 52.5% were male. The CA125 cutoff value for predicting fluid overload was >11.36 U/mL, with an AUC of 0.764 (95% CI: 0.66–0.87, p < 0.001), sensitivity of 85%, and specificity of 65%. At the cut-off point of 36.06, CA 125 had a sensitivity of 0.86 and a specificity of 0.72 in predicting in-hospital outcomes in patients with heart failure. **Conclusion**: CA125 demonstrates good accuracy in predicting fluid overload and in-hospital outcomes in patients with heart failure.

KEYWORDS: CA125, fluid overload, heart failure.

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INTRODUCTION

Heart failure is a common disease and places a heavy economic, social and public health burden on many countries. From 2017 to 2020, heart failure affected nearly 6.7 million Americans aged 20 and older[1]. It is estimated that by 2030, more than 8 million Americans will have heart failure[2]. Heart failure has many consequences if not treated well, such as reduced life expectancy, reduced quality of life, and even death. There are many means of assessing the worsening of heart failure, one of the typical signs is fluid overload. This is one of the main reasons why heart failure patients are hospitalized and is also an important goal that needs to be addressed when treating heart failure. According to a report by the European Society of Cardiology, 83% of patients hospitalized for acute heart failure have functional symptoms or physical signs of fluid overload[3]. In a global cohort study, 39.2% of Southeast Asian patients hospitalized for heart failure had peripheral edema[4]. Fluid overload is a factor associated with an increased risk of readmission and death in patients with heart failure[5]. However, the severity and distribution of fluid are highly variable between patients, which can make it difficult to predict fluid overload in patients with heart failure. In recent years, there has been increasing evidence supporting the use of carbohydrate antigen 125 (CA125) in cardiovascular disease, especially heart failure, and many studies worldwide have demonstrated a relationship between CA125 and the degree of fluid overload[6]. Prior to CA125, many other prognostic markers such as natriuretic peptide, high-sensitivity troponin, proadrenomedullin, soluble ST2, and galectin-3 have been evaluated. Despite the effectiveness of some prognostic markers, the difficulty remains in obtaining predictors that can be determined in a short time frame for patients with AHF. Economically, CA125 is much cheaper than NTproBNP. In a study by Sekan et al., when NTproBNP was used alone to predict 1-year mortality, the sensitivity was only 82%, compared with 91% when combined with CA125[7]. Therefore, we conducted the research topic "The role of CA125 in predicting fluid overload and in-hospital outcomes in patients with heart failure", from which we can propose optimal treatment strategies for patients.

Objectives: 1) To determine the AUC, cutoff value, sensitivity, specificity, positive predictive value, and negative predictive value of CA125 in predicting fluid overload in HF patients. 2) To determine the AUC, cutoff value, sensitivity, specificity, positive predictive value, and negative predictive value of CA125 in predicting in-hospital outcomes in HF patients. 3) To evaluate the independent predictive value of CA125 in assessing fluid overload and in-hospital outcomes in HF patients.

METHODS

Study design: prospective cohort study

Time and location: The study was conducted at the Department of Internal Medicine, Binh Chanh General Hospital from March 2025 to September 2025.

Exclusion criteria: Patients who are in menstrual cycle, pregnant, ovarian carcinoma, have pelvic tumors, peritonitis, pericarditis, cirrhosis, endometriosis by asking about medical history, medical history, examination and labs tests. Subjects who are not conscious, aware of the interview, do not cooperate in the data collection process. There was no result of CA125.

Data collection: demographic characteristics, cardiovascular risk factors, medical history, clinical characteristics at admission, paraclinical indices including CA125, estimated Glomerular filtration rate, Total cholesterol, LDL-C, HDL-C, Triglycerides, Echocardiography, Treatment characteristics including drug treatment and in-hospital outcome events were recorded.

Statistical analysis: Collected data will be cleaned and entered into the computer using Epidata 3.1 software. Data analysis was performed using STATA 14.0 software. ROC curve was drawn, from which the cut-off point, sensitivity, specificity were determined and the area under the curve AUC was calculated.

Medical ethics: This research has been approved by the Ethics Council in Biomedical Research of Pham Ngoc Thach University of Medicine according to certificate No.1240/TĐHYKPNT-HDDD dated 03/12/2024 and Binh Chanh General Hospital (No.03/BVBC - HDDD, signed on 04/03/2025).

RESEARCH RESULTS

General characteristics:

A total of 122 patients were included in the analysis. The mean age of the study population was 6.8.1 ± 1.3.5 years, the youngest was 34 years old and the oldest was 98 years old, the group of patients < 65 years old accounted for 37.7 %. Of which, females accounted for 47.5 %. Median BMI was 21.4 kg/m². Characteristics of cardiovascular risk factors and underlying diseases of the study population were showed in Table 1. Vital signs and echocardiographic characteristics at admission in the study population were displayed in Table 2. Labs test Results of the study population were also presented in Table 3. Treatment characteristics in the study population were showed in Table 4.

Table 1. Characteristics of cardiovascular risk factors and underlying diseases of the study population.

Characteristic	Total	Male	Female	p
Hypertension	113 (92.6%)	61 (95.3%)	52 (89.7%)	0.233*
Diabetes	49 (40.2%)	28 (43.8%)	21 (36.2%)	0.396*
Lipid disorders	111 (91.0%)	58 (90.6%)	53 (91.4%)	0.884*
History of IHD	103 (84.4%)	56 (87.5%)	47 (81.0%)	0.325*
Heart failure	98 (80.3%)	54 (84.4%)	44 (75.9%)	0.238*
Valvular heart disease	60 (49.2%)	34 (53.1%)	26 (44.8%)	0.360*
Peripheral edema	62 (50.8%)	27 (42.2%)	35 (60.3%)	**0.045***
Pleural effusion	89 (73.0%)	44 (68.8%)	45 (77.6%)	0.273*
Smoking	55 (45.1%)	52 (89.7%)	3 (4.7%)	**<0.001***
Obesity	27 (22.1%)	8 (12.5%)	19 (32.8%)	**0.007** *

*Chi-square test

Comments: Peripheral edema history in women is higher than in men, the difference is statistically significant (p=0.045). In contrast, smoking is a risk factor recorded in men, the difference is statistically significant (p<0.001). Obesity is higher in women than in men, and this difference is statistically significant (p=0.007).

Table 2. Vital signs and echocardiographic characteristics at admission in the study population.

Characteristic	Total	Male	Female	p
Heart rate, mean ± SD (min-max)	96.3 ± 20.0 (50 – 160)	95.2 ± 18.1 (50 – 130)	97.6 ± 22.0 (53 – 160)	0.623*
SBP , Mean ± SD (min-max)	137.2 ± 26.1 (80 – 220)	135.3 ± 24.2 (90 – 200)	139.3 ± 28.0 (80 – 220)	0.537*
DBP, Mean ± SD (min-max)	81.7 ± 13.7 (50 – 140)	80.5 ± 11.7 (60 – 100)	83.1 ± 15.6 (50 – 140)	0 ,470*
LVEF %, medium (IQR)	96.3 (50 – 160)	51.5 (45 – 57)	48.0 (41 – 55)	0.088*
LVEDd (mm), Mean ± SD (min-max)	50.2 ± 7.2 (35 – 70)	48.2 ± 7.2 (35 – 67)	52.4 ± 6.5 (36 – 70)	**<0.001***

*Mann-Whitney test; **Chi-square test; IQR: interquartile range; DBP: diastolic blood pressure; LVDd: diameter of left ventricular end diastolic; LVEF; left ventricular ejection fraction; SD: standard deviation, SBP: systolic blood pressure; min: minium, max: maxium

Comments: mean LVEDd in women was higher than in men and this difference was statistically significant (p<0.001). There was no statistically significant difference between the two sexes in terms of systolic blood pressure, diastolic blood pressure, and LVEF %.

Table 3. Labs test Results of the study population

Characteristic	Total	Male	Female	p
Hemoglobin (g/dL), Mean ± SD (min-max)	11.9 ± 2.1 (6.8 – 16.4)	11.6 ± 1.9 (6.8 – 16.1)	12.2 ± 2.3 (6.8 – 16.4)	0.057*
Creatinine (μmol/L), Median (IQR)	111.3 (91.3 – 143)	105.5 (85.8 – 127.1)	119.5 (101 – 162)	**0.010***
Urea (mmol/L), Median (IQR)	7.5 (4.9 – 9.6)	6.9 (4.4 – 9.0)	8.7 (5.9 – 10.2)	**0.019***
eGFR (mL/min/1.73m^2), Mean ± SD (min-max)	50.3 ± 19.6 (10.6 – 93.3)	47.2 ± 17.7 (10.7 – 91.9)	53.6 ± 21.2 (10.6 – 93.3)	0.069*
Na^+ (mmol/L), Median (IQR)	139.7 (136.7 – 141)	139.5 (136.9 – 141.6)	138.9 (136.5 – 141)	0.333*
K^+ (mmol/L), Mean ± SD (min-max)	3.8 ± 0.6 (2.0 – 5.7)	3.8 ± 0.6 (2.1 – 5.7)	3.9 ± 0.6 (2.0 – 5.1)	0.516*
Glucose (mg/dL), Median (IQR)	146 (112 – 190)	142.5 (111.5 – 187)	147.5 (111 – 199)	0.672*
Troponin I (ng/L), Median (IQR)	22.8 (9.9 – 76)	14.4 (6.9 – 49.9)	36.5 (17.5 – 226.2)	**0.002***
NT-proBNP (pg/mL), Median (IQR)	496 (220 – 1181)	460.5 (181 – 945.5)	541 (240 – 1294)	0.192*
CA125 (U/mL), Median (IQR)	26.2 (10.5 – 69.3)	26.5 (10.4 – 71.8)	26.1 (11.9 – 54.6)	0.631*

*Mann-Whitney test; IQR: interquartile range ; SD: standard deviation, min: minium, max: maxium

Comments: median creatinine levels in women was higher than in men and this difference was statistically significant (p=0.010). Median Urea levels in women was higher than in men and this difference was statistically significant (p=0.019). Median Troponin I concentration in women was higher than in men and this difference was statistically significant (p=0.002).

Table 4. Treatment characteristics in the study population

Characteristic	Total n(%)	Male n(%)	Female n(%)	p
Clopidogrel	61 (50.0%)	30 (48.4%)	30 (51.7%)	0.717*
ARNI	91 (74.6%)	45 (70.3%)	46 (79.3%)	0.254*
Beta-blockers	92 (75.4%)	52 (81.3%)	40 (69.0%)	0.116*
SGLT2	61 (50.0%)	35 (54.7%)	26 (44.8%)	0.277*
Diuretic	85 (69.7%)	45 (70.3%)	40 (69.0%)	0.872*
Aspirin	38 (31.1%)	16 (25.0%)	22 (37.9%)	0.124*
Nitrates	50 (41.0%)	26 (40.6%)	24 (41.4%)	0.933*
Anticoagulants	28 (23.0%)	17 (26.6%)	11 (19.0%)	0.319*
Statins	100 (81.9%)	51 (79.7%)	49 (84.5%)	0.491*
Fluid overload	91 (74.6%)	45 (70.3%)	46 (79.3%)	0.254*
In-hospital outcomes				
Stable, discharged	100 (82.0%)	100 (81.9%)	100 (81.9%)	0.238*
Readmission	20 (16.4%)	8 (12.5%)	12 (20.6%)	
Deaths	2 (1.6%)	2 (3.1%)	0 (0.0%)	

*Chi-square test, ARNI: Angiotensin Receptor-Neprilysin Inhibitor; SGLT2i: Sodium-Glucose cotransporter 2 inhibitor

Comments: There was no statistically significant difference between the two sexes in medication treatment upon discharge, fluid overload and in-hospital outcomes.

The AUC, cut-off point, sensitivity, specificity, positive predictive value, negative predictive value of CA125 in predicting fluid overload in patients with heart failure

With the cut-off point CA125 = 11.36, the area under the ROC curve (AUC) reached 0.764 (95% CI: 0.66 - 0.87), a statistically significant difference with p<0.001. At the cut-off point of 11.36, CA125 had a sensitivity of 0.85 and a specificity of 0.65 in predicting fluid overload in patients with heart failure. The positive predictive value reached 87.5%, while the negative predictive value reached 58.8%. Results were showed in Figure 1.

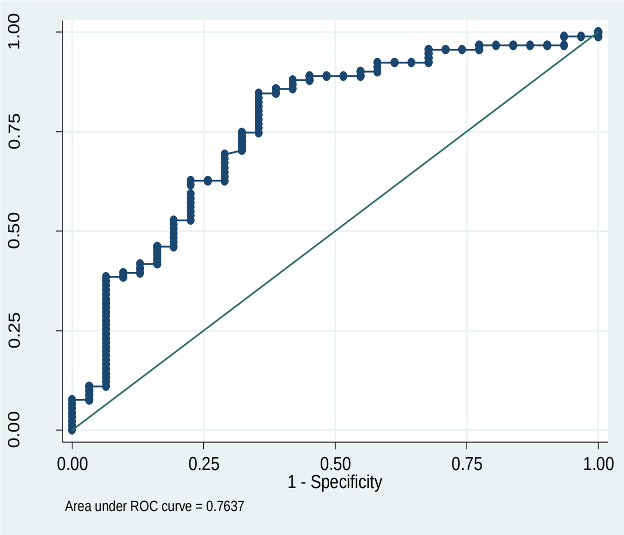

Figure 1. ROC curve of CA125 index in predicting fluid overload in patients with heart failure

The AUC, cut-off point, sensitivity, specificity, positive predictive value, negative predictive value of CA125 in predicting in-hospital outcomes in patients with heart failure

With the cut-off point CA125 = 39.06, the area under the ROC curve (AUC) reached 0.810 (95% CI: 0.72 - 0.89), a statistically significant difference with p<0.001. At the cut-off point of 36.06, CA125 had a sensitivity of 0.86 and a specificity of 0.72 in predicting in-hospital outcomes in patients with heart failure. The positive predictive value reached 40.4%, while the negative predictive value reached 96.0%. The results were displayed in Figure 2.

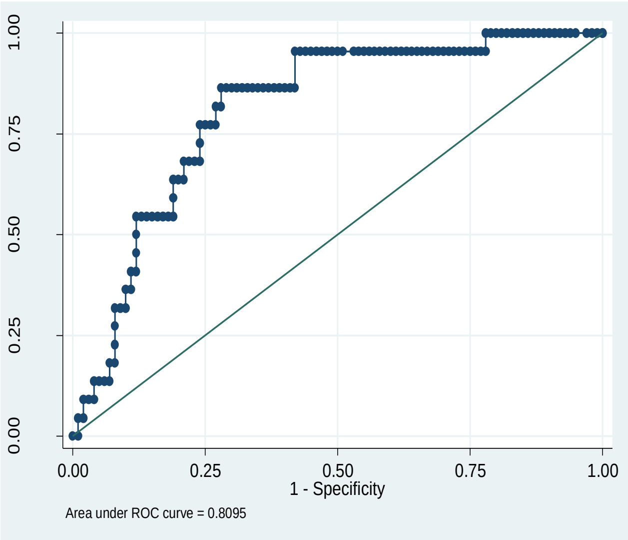

Figure 2. ROC curve of CA125 index in predicting in-hospital outcome in patients with heart failure

The independent predictive value of CA125 in predicting fluid overload and in-hospital outcomes in patients with heart failure

Table 5. Independent predictive value of CA125 in predicting fluid overload in patients with heart failure (n=122)

CA125 (U/mml)	Fluid overload n(%)	Without Fluid overload n(%)	RR	95%CI	p*
≥ 35	44 (48.4)	6 (19.4)	2.5	1.2 – 5.3	0.005
< 35	47 (51.7)	25 (80.6)			
Total	91 (100.0)	31 (100.0)			

*Chi-square test; CI: confidence interval; RR: Relative Risk

Comment: There is a correlation between CA125 values and fluid overload characteristics in heart failure patients, specifically patients with CA125 level ≥ 35 U/ml have a fluid overload rate 2.5 times higher than the group of patients with CA125 level < 35 U/ml. This difference is statistically significant with p=0.005. Results were showed in Table 5.

Table 6. Independent predictive value of CA125 in predicting in-hospital outcomes in patients with heart failure (n=122)

CA125	In-hospital outcomes		RR	95% CI	p*
	Death and Readmission n(%)	Discharge n(%)			
≥ 35	19 (86.4)	31 (31.0)	2.8	2.0 – 3.9	<0.001
< 35	3 (13.6)	69 (69.0)			
Total	22 (100.0)	100 (100,0)			

*Chi-square test; CI: confidence interval; RR: Relative Risk

Comments: There is a correlation between CA125 values and in-hospital outcomes in patients with heart failure. Specifically, patients with CA125 index ≥ 35 U/ml have a 2.8 times higher rate of poor in-hospital outcomes than patients with CA125 index < 35 U/ml. This difference is statistically significant with p<0.001. Results were showed in Table 6.

DISCUSSION

In our study, 122 patients with heart failure who met the inclusion and exclusion criteria were included in the study. Our study recorded an average age of 68.1 ± 13.5 years, reflecting the common characteristics of the heart failure patient population. mainly in the elderly group. This result is similar to the study of Núñez et al. (2016), in which the mean age of patients with acute heart failure was 70.2 ± 12.8 years[8], and the study of Miñana et al. in 2022 on patients with heart failure with preserved ejection fraction with a mean age of 67 ± 11 years[9] . When analyzing gender characteristics, our study results showed that men accounted for a higher proportion than women (52.5% vs. 47.5%), with a male:female ratio of approximately 1:1. In our study, the proportion of non-smoking patients accounted for 54.9%, higher than the smoking group. This shows a decreasing trend in smoking rates among heart failure patients, which may reflect the effectiveness of tobacco control programs and increased public awareness of the harmful effects of smoking on the cardiovascular system in recent years. This result is different from the study by Shi et al. (2020), in which the proportion of non-smoking patients was only 36.3%[10] , suggesting that in some populations, especially in Asia, smoking habits are still common among patients with cardiovascular disease.

Regarding underlying diseases, our study showed that hypertension was the most common disease with 92.6%, followed by lipid disorders (91.0%) and a history of IHD was 84.4%. This underlying disease structure suggests that the population carries a large metabolic and coronary burden, reflecting the fundamental role of hypertension and lipid disorders in the pathogenesis of heart failure. Our results are similar in trend to other large studies such as Zhang et al. (2023), Núñez et al. (2016), who also reported hypertension as the most common underlying disease in heart failure populations[11]. However, the prevalence of IHD in the current study (84.4%) was significantly higher than that reported by Zhang et al. (18.2%), suggesting a large difference in study sample characteristics or inclusion criteria between studies.

Regarding the paraclinical characteristics in our study, the results of blood count tests showed that the average Hemoglobin (Hb) concentration of heart failure patients was recorded as 11.9 ± 2.1 g/dL, which is within the low normal range. This shows that most patients did not have severe anemia at the time of the survey, although mild anemia was still present in some cases. This result is similar to the study of Núñez et al. (2016), when the authors reported an average Hb of 12.1 ± 1.9 g/dL in patients with heart failure[8] . Zhang et al. (2023) also recorded similar results with an average Hb value of 12.0 ± 2.2 g/dL[11], indicating that mild anemia is quite common in heart failure patients worldwide.

Regarding the results of blood biochemistry tests, our study recorded the median serum creatinine concentration of 111.3 µmol/L (IQR: 91.3 – 143), indicating that a significant proportion of patients had mild to moderate renal impairment. The median urea concentration reached 7.5 mmol/L (IQR: 4.8 – 9.6), which is within the upper limit of the reference value, reflecting the influence of hemodynamic disorders and renal hypoperfusion commonly found in patients with heart failure. The mean estimated glomerular filtration rate (eGFR) was 50.3 ± 19.6 mL/min/1.73m², suggesting that most patients had chronic renal failure stage 2–3 according to the KDIGO classification. This result is consistent with many international studies. In the CHANCE-HF study by Núñez et al. (2016), the mean creatinine concentration was recorded at 115 ± 46 µmol/L, with a mean eGFR of 52 ± 20 mL/min/1.73m^2 [8] , indicating a similar degree of renal impairment. Miñana et al. (2022) also reported a mean creatinine of 108 ± 39 µmol/L and an eGFR of 54 ± 18 mL/min/1.73m², reflecting similarities between acute heart failure patient populations in Europe and Asia[9]. In 2023 Zi Zhang et al recorded an average creatinine of 109 (79–140) µmol/L similar to our results[12]. This shows a close correlation between heart failure and renal dysfunction in Vietnamese patients, especially in the context of high rates of underlying diseases such as hypertension, diabetes and lipid disorders.

In our study, the specific biomarkers for cardiac injury and overload, including Troponin I, NT-proBNP, and CA125, had median and IQR of 22.8 (9.9 – 76) ng/L, 496 (220 – 1181) pg/mL, and 26.2 (10.5 – 69.3) U/mL, respectively. Overall, the median values of these markers were within normal limits, indicating that most of the patients in the study were not in the stage of acute decompensated heart failure at the time of sample collection. This result is similar to the study of Núñez et al. (2016), in which the median Troponin I was 28 ng/L and the median NTproBNP was about 560 pg/mL[8] , reflecting mild to moderate myocardial injury in patients with stable chronic heart failure. Zhang et al (2023) also reported a median NTproBNP of 510 pg/mL, similar to our results, but noted higher Troponin I (median 45 ng/L)[11], possibly because their study population included many patients with acute decompensated heart failure or concomitant coronary artery disease.

For CA125, our results (26.2 U/mL) were comparable to those reported by Miñana et al. (2022) with a mean value of 27.8 U/mL in patients with stable chronic heart failure[9] , and significantly lower than the study by Truong Minh Chau (2025)[13], in which the mean CA125 was up to 70.0 U/mL in the group of patients with acute heart failure with severe fluid retention and a fatal prognosis. This suggests that CA125 is closely related to congestion and extracellular fluid volume, indirectly reflecting the severity of heart failure and can be used as an indicator to monitor treatment response.

Regarding echocardiographic indicators, our study recorded a median left ventricular ejection fraction (LVEF%) of 50% (IQR 43 - 56%), showing that most patients had preserved or slightly reduced left ventricular contractile function. This result is consistent with the characteristics of the group of heart failure with preserved or intermediate ejection fraction, commonly found in the elderly, women and patients with chronic hypertension. The left ventricular end-diastolic diameter (LVDd) in the study had an average value of 50.2 ± 7.2 mm, within the normal to mild dilation range, reflecting a degree of myocardial remodeling that was not too severe. This result is similar to the study of Núñez et al. (2016) with an average LVEF of 44.7 ± 17.2 % [8] . Truong Minh Chau's study reported LVEF 42.5 ± 16.4%, showing that the patient population had moderate heart failure, mainly in the intermediate ejection fraction heart failure group[13].

In our study, the proportion of patients with fluid overload was 74.6%, indicating that most patients were admitted in a congestive state. This result is similar to the study of Ambrosy et al. (2014) on patients with acute heart failure, which noted that about 90% of hospitalized patients had signs of congestion. In Asia, the study of Miñana et al. (2022) also showed that over 70% of heart failure patients had clinical or paraclinical evidence of fluid retention, similar to our results[9].

This shows that fluid overload not only aggravates symptoms of dyspnea and peripheral edema, but is also closely related to an unfavorable prognosis, including increased risk of rehospitalization and death. Therefore, early assessment and control of fluid overload plays a key role in the management of heart failure patients, helping to improve quality of life and reduce the burden of long-term treatment.

Through analysis of the results, we noted that the majority of patients were discharged in stable condition (82.0%), while the readmission rate was 16.4% and in-hospital mortality was 1.6%. These figures indicate that the majority of patients were effectively treated and safely discharged; however, the readmission rate is still noteworthy as a challenge in post-discharge management. In addition, the mortality rate of our study was lower than many international studies. Specifically, the study by Ambrosy et al. (2014) on data from the EVEREST trial recorded an average in-hospital mortality rate of 4.0%[14] . In Vietnam, the study by Truong Minh Chau reported a high mortality rate of 25.6%[13] . In contrast, the study by Shi et al.,[10] which followed 2079 patients for 21 months and at the end of the study, recorded a mortality rate of 3.6%, similar to our study. Although the in-hospital mortality rate was low, the readmission rate of 16.4% was still a concern. This result is similar to the study by Truong Minh Chau with a readmission rate of 20.2%[13] , showing that re-congestion and adherence to treatment after discharge are major challenges in heart failure management. Therefore, enhancing post-discharge care, educating patients about diet, medication and self-monitoring of weight, and early follow-up visits after 7–14 days are important measures to reduce readmissions and improve long-term prognosis.

In our study, CA125 concentration had significant diagnostic value in predicting fluid overload in patients with heart failure, with the area under the ROC curve (AUC) reaching 0.764 (95% CI: 0.66 - 0.87; $p < 0.001$). At the cut-off threshold of 11.36 U/mL, CA125 had a sensitivity of 85% and a specificity of 65%, with a positive predictive value of 87.5% and a negative predictive value of 58.8%. This result confirmed that CA125 is a highly sensitive marker, suitable for screening and early identification of fluid overload in hospitalized patients with heart failure. Compared with other studies, our results were higher than those of Durak-Nalbantic et al. (2023)[15] with AUC 0.59 , sensitivity of 60.5% and specificity of 53.3%, with a positive predictive value of 64.5% at the threshold of 80.5 IU/L. This difference may be explained by the characteristics of the study population and different disease stages. In Vietnam, Phan Thai Hao et al[11] recorded the area under the ROC curve (AUC) of CA125 in predicting fluid overload as 0.717, lower than our results (AUC = 0.764). At the cutoff threshold >16 U/mL, the sensitivity reached 85.6% and the specificity was 56.2% [16], showing that this result was similar in trend to our study when it was also noted that CA125 is a sensitive marker in detecting fluid overload in patients with heart failure.

In our study, at the cut-off threshold of CA125 = 39.06 U/mL, the area under the ROC curve (AUC) reached 0.810 (95% CI: 0.72–0.89), a statistically significant difference ($p < 0.001$). At this threshold, CA125 had a sensitivity of 86% and a specificity of 72%, with a positive predictive value of 40.4%, showing the ability to clearly differentiate between the group of patients with poor in-hospital outcomes and the stable group.

The results of our study had a lower CA125 cutoff than the study of Zhang et al. (2023)[12], in which the authors noted that patients with CA125 ≥ 65.7 U/mL had a significantly higher 1-year mortality rate. Similarly, the study of Shi et al. (2020)[10] showed that AUC 0.63 in predicting mortality in patients with heart failure, which was lower than our results (AUC = 0.810). This difference may be explained by the characteristics of the study population and the severity of heart failure. In the study of Zhang and Shi, most of the subjects were patients with advanced heart failure (NYHA III–IV) or heart failure with reduced ejection fraction, resulting in higher CA125 concentrations and a larger optimal cutoff point. In contrast, our study included both acute and chronic heart failure groups with moderate congestion, so the CA125 threshold was lower but the predictive ability (AUC) was higher, reflecting the sensitivity of this marker in early detection of fluid overload and short-term prognosis.

In Vietnam, Truong Minh Chau et al [13] also reported that CA125=113 U/mL was the optimal cutoff point for predicting cardiovascular death, with a sensitivity of 60.5% and a specificity of 73.0%, significantly higher than our cutoff. This difference may be due to the author's study focusing on the population of patients with severe heart failure admitted to the end-line hospital, where congestion, inflammation, and target organ damage are more pronounced, leading to increased CA125 levels and higher cutoff points.

Thus, although the absolute value of CA125 cut-off points varied among studies, the general trend confirmed that increased CA125 concentrations were closely associated with worse prognosis, including in-hospital and post-discharge mortality, suggesting the potential of this marker as an independent predictor in risk assessment in patients with heart failure.

When analyzing the relationship between CA125 concentration and fluid overload, our study results showed that CA125 has significant prognostic value. Specifically, the group of patients with CA125 concentration ≥ 35 U/mL had a 2.5 times higher risk of fluid overload than the group with CA125 < 35 U/mL ($p < 0.001$). This result is consistent with international studies, such as the study of D'Aloia et al. (2003) showing that increased CA125 concentration is closely related to the degree of central venous congestion and increased pulmonary capillary pressure, reflecting fluid retention in patients with chronic heart failure. Similarly, Núñez et al. (2016)[8] also confirmed that the CA125 threshold > 35 U/mL is valuable in risk stratification and prediction of clinical events in patients with heart failure . Overall, domestic and foreign evidence reinforces the role of CA125 as a biomarker reflecting congestion and fluid overload, and is also a useful support in the clinical assessment and monitoring of heart failure patients.

In our study, there was a statistically significant correlation between CA125 values and in-hospital outcomes in patients with heart failure. Specifically, patients with CA125 ≥ 35 U/ml had a 2.8 times higher rate of poor in-hospital outcomes than the group of patients with CA125 < 35 U/ml. This shows that CA125 is not only a marker reflecting congestion and fluid overload, but also an important prognostic indicator for disease progression in the acute phase. This difference can be explained by the characteristics of the study population, the severity of heart failure, and the criteria for assessing in-hospital outcomes. In our study, the proportion of heart failure patients with reduced ejection fraction was higher, and the mean NTproBNP and creatinine concentrations were also higher, reflecting more severe congestion and hemodynamic disturbances. This is a factor contributing to increased CA125 concentrations and worsening in-hospital outcomes.

Our results are also consistent with the study of Núñez et al. (2016)[8], which showed that elevated CA125 was closely associated with the severity of heart failure, prolonged hospital stay, and higher mortality one year after discharge. The authors suggested that CA125 not only reflects venous congestion but is also related to systemic inflammatory response and endothelial damage, two mechanisms that play a central role in the progression of heart failure[8]. Thus, our study results contribute to strengthening the evidence for the role of CA125 as a multidimensional biomarker, not only reflecting congestion but also having independent prognostic value for in-hospital outcomes in patients with heart failure. Determining the threshold of CA125 ≥ 35 U/mL may be useful in risk classification, monitoring treatment response and early prediction of adverse events during hospitalization.

CONCLUSION

With the cut-off point CA125 = 11.36, the area under the ROC curve (AUC) reached 0.764 (95% CI: 0.66 - 0.87), a statistically significant difference with $p<0.001$. At the cut-off point of 11.36, CA125 had a sensitivity of 0.85 and a specificity of 0.65 in predicting fluid overload in patients with heart failure. The positive predictive value reached 87.5%, while the negative predictive value reached 58.8%.

With the cut-off point CA125 = 39.06, the area under the ROC curve (AUC) reached 0.810 (95% CI: 0.72 - 0.89), a statistically significant difference with $p<0.001$. At the cut-off point of 36.06, CA125 had a sensitivity of 0.86 and a specificity of 0.72 in predicting in-hospital outcomes in patients with heart failure. The positive predictive value reached 40.4%, while the negative predictive value reached 96.0% statistically significant correlation between CA125 values and fluid overload characteristics in heart failure patients. Specifically, patients with CA125 index ≥ 35 U/ml had a fluid overload rate 2.5 times higher than the group of patients with CA125 index < 35 U/ml.

There was a statistically significant association between CA125 values and in-hospital outcomes in patients with heart failure. Specifically, patients with CA125 levels ≥ 35 U/ml had a 2.8-fold higher rate of poor in-hospital outcomes than patients with CA125 levels < 35 U/ml.

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