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Letter to the Editor

Prognostic value of CA125 in advanced heart failure patients

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Abstract

Introduction: Serum levels of CA125 are often high in advanced heart failure (AHF) patients.**Aim:** To determine the predictive value of CA125 in forecasting the occurrence of death or cardiac transplantation in an AHF population.**Methods:** 88 AHF patients referred for heart transplantation were divided into 2 groups based on CA125 levels: normal (CA125 < 38 U/mL) and elevated (≥ 38 U/mL). Events (death or heart transplant) were monitored over a period of 13 ± 7 months after CA125 determination.**Results:** Patients with elevated CA125 ($n=65$) had significantly lower blood pressure, body mass index, serum sodium and peak exercise oxygen consumption, while B-type natriuretic peptide levels were significantly higher. The combined primary endpoint (death or heart transplant) rate was 39.4% and 62.3% in normal and elevated CA125 groups, respectively ($p=0.029$). Multivariate regression analysis showed that CA125 and sodium levels were the only independent predictors of the combined endpoint.**Conclusion:** In AHF patients, plasma CA125 was an effective prognostic marker. Its determination may contribute to better risk stratification in this population.

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1. Introduction

Advanced heart failure (AHF) is associated with high morbidity and mortality rates [1–3], unless cardiac transplantation is performed. Risk stratification of AHF patients is a critical component of the transplant candidate selection process; therefore, search for new prognostic markers in AHF has recently been intensified.

Carbohydrate antigen 125 (CA125) is a tumour marker classically associated with ovarian cancer [4]; recently several studies reported increased serum CA125 levels in HF patients [5–15].

Table 1

Clinical characteristics of the study population of advanced heart failure patients ($n=88$)

Age (years)	53.5 \pm 13.8
Men/women	62 (70%)/26 (30%)
Body mass index (kg/m ²)	24.0 \pm 5.0
LVEF (%)	24.5 \pm 11.2
NYHA functional class (%)	
III	58.1
IV	41.9
Aetiology (%)	
Dilated cardiomyopathy	49
Coronary artery disease	40
Hypertensive heart disease	10
Other	1

Data are presented as the mean value \pm SD, number or percentage of patients. LVEF — left ventricular ejection fraction; NYHA — New York Heart Association.

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Table 2

Clinical, laboratory and echocardiographic parameters of advanced heart failure patients, classified according to CA125 levels

	CA125 < 38 U/mL	CA125 ≥ 38 U/mL	<i>p</i>
Heart rate (bpm)	73.8 ± 11.5	83.1 ± 15.3	0.015
SBP (mmHg)	109.8 ± 17.7	97.0 ± 14.6	0.006
DBP (mmHg)	66.1 ± 13.8	56.7 ± 10.3	0.01
Body mass index (kg/m ²)	24.8 ± 6.5	23.4 ± 3.2	0.04
Serum Sodium (mmol/L)	135.9 ± 4.5	133.9 ± 4.1	0.04
Serum creatinine (mg/dL)	1.4 ± 0.5	1.7 ± 1.7	0.80
BNP (pg/mL)	593.4 ± 554.9	2180.1 ± 1468.7	<0.001
LVEF (%)	24.7 ± 11.5	24.3 ± 11.1	0.92
Peak VO ₂ (mL/kg/min)	16.0 ± 5.1	13.8 ± 3.4	0.049

SBP — systolic blood pressure; DBP — diastolic blood pressure; BNP — B type natriuretic peptide; LVEF — left ventricular ejection fraction; Peak VO₂ — peak exercise oxygen consumption.

However, it is still a matter of debate if CA125 is a potential prognostic marker for AHF and also if it is useful for evaluating and managing pre-transplant patients.

The aim of the present study was to determine the predictive value of plasma CA125 in forecasting the occurrence of death or cardiac transplantation in an AHF patient population.

1.1. Patients and methods

This study included 88 consecutive AHF patients referred for heart transplantation (62 male, mean age 53.5 ± 13.8 years) — Table 1.

CA125 assays were performed during clinic visits or during hospitalization for HF, after clinical stabilization (7 ± 3 days). Serum levels of CA125 were measured by chemiluminescence (BRAHMS CA125 II KRYPTOR), with an upper normal limit

of 38 U/mL. Population was divided into two groups according to CA125 levels: normal (CA125 < 38 U/mL) and elevated (≥ 38 U/mL).

Patients were followed for a mean period of 13 ± 7 months after CA125 assessment; the study primary endpoint was death or heart transplant.

1.2. Statistical analysis

Data are presented as the mean value ± SD. Analysis of groups differences was performed using the Mann–Whitney *U* test for continuous variables and χ^2 test for categorical variables. A *p* value < 0.05 was considered statistically significant. Survival curves were constructed by the Kaplan–Meier method and were compared using the log-rank test. Multivariate regression analysis was then performed to determine the independent predictors of the primary endpoint.

2. Results

Twenty-three patients had normal CA125 (15.3 ± 6.1 U/mL), while 65 had elevated levels (215.6 ± 260.2 U/mL). Groups were similar regarding demographic characteristics, HF aetiology and medication.

Compared to the normal group, patients with elevated CA125 had significantly lower systolic and diastolic blood pressure, body mass index, serum sodium and peak oxygen consumption in the cardio-respiratory stress test. B-type natriuretic peptide (BNP) levels were also significantly higher in this group (Table 2).

In elevated CA125 group, 38% of patients had pleural effusion *versus* none in normal CA125 group (*p* = 0.014).

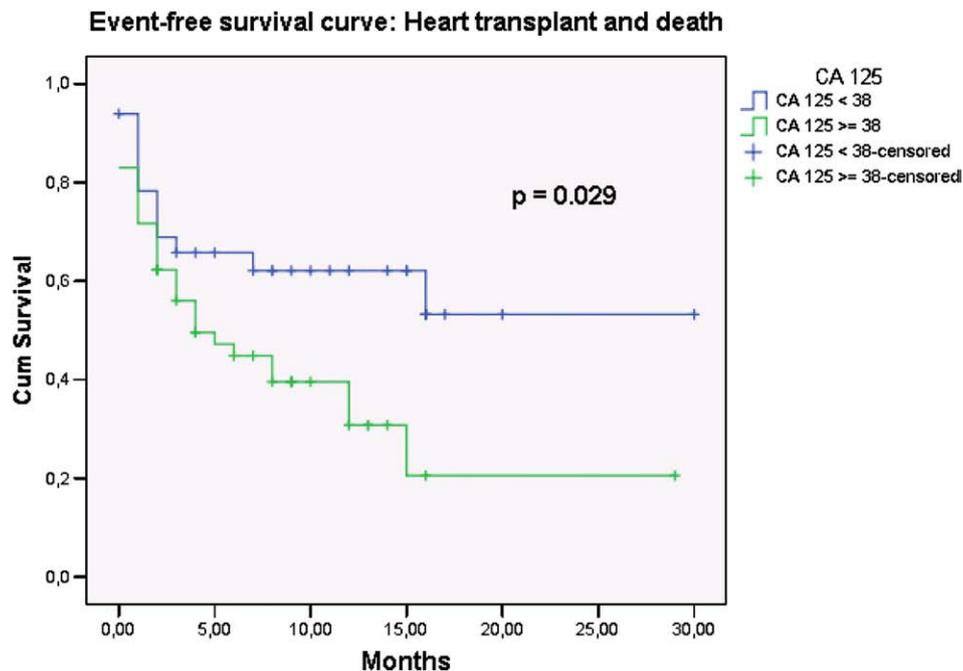


Fig. 1. Kaplan–Meier cumulative event-free survival curves separated according to CA125 levels.

Table 3
Multiple regression analysis

Variables	Beta	p-value	OR
CA125 ≥ 38 U/mL	1.152	0.032	3.163 (1.107–9.036)
NA ≤ 132.5 mmol/L	1.339	0.041	3.817 (1.056–13.799)

c-statistic 0.728.

Event rate was significantly lower in patients with normal CA125 levels: 2 versus 15 died, 11 versus 19 were transplanted and 13 versus 27 were readmitted for worsening HF. The combined primary endpoint (death or heart transplant) rate was 39.4% in patients with normal CA125 values and 62.3% in the elevated CA125 group ($p=0.029$) — Fig. 1.

Multivariate regression analysis showed that CA125 and sodium levels were the only independent predictors of the combined endpoint (Table 3).

3. Discussion

Numerous studies showed increased CA125 levels in CHF patients and a relationship between these values and HF severity [5–15]. In the present study, we investigated the prognostic value of CA125 levels in an AHF population.

According to our results, serum CA125 was elevated in most AHF patients and its levels were significantly related to blood pressure, body mass index, serum sodium, peak exercise oxygen consumption and BNP levels (established markers of severity and prognosis in HF).

We did not find significant differences in LVEF between patients with normal and elevated CA125, probably because our population included mainly severe AHF patients with low LVEF ($24.5 \pm 11.2\%$) and LVEF is not a good marker to stratify AHF patients [1].

Our data clearly demonstrated that CA125 is a marker of adverse outcome in AHF patients, associated with increased mortality, transplant and hospital readmission rates. Multivariate analysis identified CA125 as an independent predictor for the combined endpoint death or heart transplant.

In several reports high CA125 was associated with serosal effusions, suggesting that the presence of serosal fluids may stimulate its release [8–10].

However, other investigators showed increased CA125 levels in HF patients without serosal effusion, indicating that an acute congestion may not be the sole cause of CA125 secretion [6,7].

The majority of our patients with high CA125 did not have pleural effusion, either because they were clinically stable or because many AHF patients do not have serosal effusions.

Recently, Kosar [16] demonstrated that high CA125 levels in HF patients were correlated with inflammatory cytokines levels, suggesting a relationship between CA125 and cytokines.

As in our study CA125 was measured during routine clinic visits or in hospitalized patients (but after clinical

stabilization), our results support the hypothesis that CA125 is an effective marker of AHF severity and prognosis, even in compensated phases of the disease.

4. Conclusion

In AHF patients, CA125 is an independent predictor of worse prognosis, associated with a higher event rate and increased mortality. Even in stable patients CA125 is a useful marker of AHF severity and prognosis, which can be used to improve risk stratification and guide therapeutic decisions.

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The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology [17].

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