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Admission Serum Creatinine/Albumin Ratio and its Relationship with 1-Year Mortality in Decompensated Heart Failure Patients

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Abstract

Aim: Despite medical advancements, heart failure (HF) maintains high mortality rates. Our research delves into examining the relationship between the serum creatinine/albumin ratio and one-year mortality in patients with decompensated systolic HF.

Methods: During the period from October 2014 to October 2015, we enrolled 80 patients (comprising 37 females) who had been diagnosed with acute systolic decompensated heart failure and had a left ventricular ejection fraction (LVEF) of ≤ 40%. These patients were divided into two cohorts depending on whether they experienced all-cause mortality within the span of one year.

Results: Among the 80 participants, 31 (39%) experienced mortality within the first year. The average age of the deceased group was 69±14 years, with 38.7% (n=12) being female. In contrast, the surviving group had an average age of 66±12 years, with 51% (n=25) being female. The HF group with mortality exhibited significantly higher levels of serum creatinine-albumin ratio, urea, and creatinine values, along with a higher prevalence of pretibial edema (p<0.01).Furthermore, the deceased HF group exhibited significantly lower LVEF, albumin levels, lymphocyte counts, and systolic and diastolic blood pressure values. Statistical analysis revealed a significant difference in the serum creatinine/albumin ratio between the deceased group (0.68±0.27) and the surviving group (0.38±0.18), with a p-value of less than 0.01. Using a cut-off value of 0.45 for the creatinine/albumin ratio, the sensitivity and specificity for predicting one-year mortality in HF patients were 81% and 78% , respectively.

Conclusion: The conjunction of heightened creatinine levels, diminished albumin levels, and an augmented creatinine/albumin ratio could potentially function as straightforward, economical prognostic indicators for forecasting one-year mortality in systolic decompensated HF patients.

Keywords: Albumin, creatinine/albumin ratio, creatinine, heart failure, mortality

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Dekompanse Kalp Yetmezliği Hastalarında Başvuru Serum Kreatinin/Albümin Oranı ve 1 Yıllık Mortalite ile İlişkisi

Öz

Amaç: Tıbbi gelişmelere rağmen kalp yetmezliği (KY) yüksek mortalite oranlarını korumaktadır. Araştırmamız, dekompensesistolik KY hastalarında serum kreatinin/albumin oranı ile bir yıllık mortalite arasındaki ilişkiyi incelemeye odaklanmaktadır.

Yöntemler: Ekim 2014 ile Ekim 2015 tarihleri arasında akut sistolikdekompanse KY tanısı konmuş ve sol ventrikülejeksiyon fraksiyonu (LVEF) ≤ 40% olan 80 hasta (37 kadın) çalışmamıza dahil edildi. Hastalar, bir yıl içinde tüm nedenlere bağlı mortalite olup olmadığına göre iki gruba ayrıldı.

Bulgular: 80 katılımcının 31'i (%39), birinci yıl içinde ölümle sonuçlandı. Ölen grubun ortalama yaşı 69±14 yıl olup, bunların %38,7'si (n=12) kadındı. Buna karşılık, hayatta kalan grupta ortalama yaş 66±12 yıl olup, bunların %51'i (n=25) kadındı. Mortalite yaşanan KY grubu, serum kreatinin-albümin oranı, üre ve kreatinin değerlerinde anlamlı düzeyde daha yüksek seviyeleri sergiledi ve pretibial ödem prevalansı daha yüksekti ($p<0.01$). Ayrıca, ölen KY grubu, LVEF, albumin seviyeleri, lenfosit sayısı, sistolik ve diyastolik kan basıncı değerlerini anlamlı derecede düşük gösterdi. İstatistiksel analiz, ölen grup (0.68±0.27) ile sağ kalan grup (0.38±0.18) arasında serum kreatinin/albumin oranı açısından anlamlı bir farklılık olduğunu gösterdi, $p<0.01$ idi. Serum kreatinin/albumin oranı için 0.45 kesme değeri kullanarak, KY hastalarındaki bir yıl içindeki mortaliteyi tahmin etmek için duyarlılık ve özgüllük sırasıyla %81 ve %78 idi.

Sonuç: Yüksek kreatinin seviyeleri, azalmış albumin seviyeleri ve artmış kreatinin/albumin oranının birleşimi, sistolikdekompenseKY'li hastalarda bir yıllık tüm nedenlere bağlı mortaliteyi öngörmede basit, ekonomik prognostik göstergeler olarak işlev görebilir.

Anahtar kelimeler: Albümin, kreatinin, kreatinin/albümin oranı, kalp yetmezliği, mortalite.

INTRODUCTION

Heart failure (HF) is a multifaceted clinical condition marked by irregularities in structure or function that impede ventricular filling and pumping capabilities, alongside corresponding hemodynamic, renal, and neurohormonal reactions[1]. HF, arising as a consequence of most cardiovascular diseases, continues to be a leading cause of morbidity and mortality[2]. While death rates from coronary artery disease (CAD) and cardiovascular diseases related to hypertension decrease with age, the incidence and prevalence of HF show an increasing trend. Among the primary causes of this increase are the growing elderly population and advancements in the diagnosis and treatment of cardiovascular diseases[3].

HF is characterized by increased mortality, progression of symptoms, and frequent hospitalizations. Approximately 60% of patients cannot survive beyond five years, and 30-40% face either death or the need for readmission within one year. In conclusion, HF represents a complex condition that emerges as a significant consequence of cardiovascular diseases[4]. The disturbances in cardiac functions lead to hemodynamic, renal, and neurohormonal responses. The increasing prevalence with age and high mortality rates underscore the severity of this disease. Therefore, a multidisciplinary approach is essential for the clinical assessment and management of HF patients[5].

HF refers to a clinical condition stemming from acute or chronic dysfunction of the heart's functions, resulting in symptoms when the heart's stroke volume fails to meet the body's demands. HF commonly emerges in the advanced stages of heart disease, affecting quality of life and leading to high mortality rates. Its prevalence varies among countries and tends to increase with age[6]. The rise in HF incidence is associated with increased life expectancy and more effective treatments for heart diseases. Advanced age, diabetes, and kidney insufficiency are predictive of mortality in HF patients. Moreover, indicators such as high creatinine levels, low albumin levels,elevated NYHA clinical class, uric acid, and C-reactive protein are also linked to increased mortality risk[7].

Albumin is the most abundant protein in the body, and reduced levels are associated with malnutrition, inflammation, and other factors. It has been observed that low albumin levels in HF patients increase the risk of mortality in both short and long terms[7]. Additionally, elevated creatinine levels are important in predicting mortality in HF patients. The deterioration of kidney function is a common occurrence in HF patients due to various mechanisms. Reduced cardiac output can lead to impaired renal perfusion, while factors like increased venous congestion, elevated intra-abdominal pressure, and activation of neurohormonal and inflammatory mediators also play a role. Furthermore, drugs like diuretics, spironolactone, and ACE inhibitors can lead to kidney function impairment through different mechanisms[8]. This situation can escalate treatment costs and increase the risk of death[9].

Numerous studies have demonstrated that low albumin levels and high creatinine levels increase the likelihood of unfavorable cardiovascular outcomes in patients with chronic congestive HF[10]. However, there are no sufficient data for patients with acute decompensated HF. Consequently, our aim was to investigate whether the ratio of routinely measured and cost-neutral creatinine and albumin values in acute decompensated HF patients could be used to predict mortality risk.

METHODS

Patient Group Selection and Data Collection

The study comprised individuals diagnosed with decompensated HF based on anamnesis, physical examination, telecardiography, electrocardiography, biochemical parameters, and proBNP levels, who were admitted to the Department of Cardiology, between October 2014 and October 2015. We prospectively enrolled 80 consecutive patients with a left ventricular ejection fraction (LVEF) of 40% or lower and followed them for one year to assess mortality as the endpoint. The research received approval from the Dicle University Ethics Committee (dated 27 November 2015, numbered 221) and consisted of individuals admitted to the hospital with a diagnosis of HF. Necessary permissions were obtained from participants.

Inclusion and Exclusion Criteria for Study Participants

Patient histories were taken, and physical examinations were performed. Patients displaying symptoms of acute decompensated HF were selected. Routine complete blood counts, biochemical tests, electrocardiography, and echocardiography were conducted for participants. The inclusion criteria were as follows: LVEF of 40% or lower and presence of at least one sign of congestion (rale, pretibial edema, venous distension, ascites, pleural effusion, etc.).

Exclusion criteria included pregnancy, end-stage kidney failure (GFR ≤ 30), diseases causing malnutrition, trauma or surgical history within the last month, being under 18 years of age, experiencing acute coronary syndrome in the last month, acute infection, known cancer, connective tissue disease, chronic liver disease.

Within the scope of the study, patients with signs of congestion and LVEF of 40% or lower were considered to have acute decompensated HF[11]. Furthermore, individuals with a blood pressure reading of ≥140/90 mmHg or those prescribed antihypertensive medications were classified as hypertensive, and those with LDL cholesterol levels >130 mg/dL or using lipid-lowering drugs were classified as having hyperlipidemia. All participants received detailed information regarding the study, and upon obtaining their consent, they were enrolled in the research.

Follow-Up and Data Analysis

Patients requiring coronary intensive care unit or clinical hospitalization due to acute

decompensated HF were monitored. Their medical histories were recorded, and physical examinations were performed. These data, along with vital signs and electrocardiographic features, were recorded electronically. Routine test results conducted during hospitalization were extracted from the hospital information system, including hemogram parameters, biochemical parameters, thyroid function tests, liver function tests, serum lipoprotein levels, albumin, blood urea nitrogen, and creatinine values. Serum albumin levels were determined utilizing the Beckman Coulter CX9 device, with the hospital's established normal range set at 3.5-5.5 g/dL. Complete blood count measurements were conducted automatically using the Abbott Cell-Dyn 3700 device. Patients were classified as survivors or deceased based on their vital status at the end of the one-year follow-up period.

Echocardiography

All patients underwent transthoracic echocardiography while positioned in the left lateral supine position using a Vivid S6 machine (Dimension/Vivid S6 Pro, Horten, Norway) equipped with a 3 MHz adult probe. Left ventricular systolic and diastolic functions were evaluated according to the American Society of Echocardiography criteria. LVEF was measured and recorded utilizing the Simpson method based on apical four-chamber and apical two-chamber images.

Statistical Analyses

For all variables, the mean and standard deviation values were provided. Statistical analyses were performed utilizing the SPSS 18 software (Statistical Package for Social Sciences, Chicago, IL, USA). Numerical data were examined for normal distribution using the Kolmogorov-Smirnov test. Student's t-test was utilized for normally distributed numerical data among independent groups, whereas the Mann-Whitney U test was employed for non-normally distributed numerical data. Categorical data between groups were compared using either the Chi-square test or Fisher's Exact Test. Additionally, receiver operating characteristic (ROC) analysis was conducted to assess mortality and identify the optimal cut-off value for the serum albumin/creatinine ratio. A p-value < 0.05 was considered statistically significant.

RESULTS

Eighty HF cases were included in the study [%54 were male (n=43); %46 were female (n=37)]. These patients were followed up for one year and were categorized into two groups: survivors and all-cause mortality.

Comparison of demographic and clinical characteristics between the two groups, including age (p=0.31), gender (p=0.28), hypertension (p=0.16), diabetes mellitus (p=0.82), hyperlipidemia (p=0.93), history of coronary artery disease(p=0.19), and history of bypass surgery (p=0.19), did not reveal any statistically significant differences (p > 0.05). According to physical examination results, the presence of pretibial edema was significantly higher in the not surviving group (p= 0.005, 87% vs. 57%, respectively) (Table I). According to the laboratory results, while albumin (p < 0.001) and lymphocyte levels (p = 0.04) were statistically higher in the surviving group, urea (p < 0.01), creatinine (p < 0.01), and the serum creatinine/albumin ratio (p < 0.01) were statistically higher in the non-surviving group (Table II).

Table I: Demographic and physical examination findings of the groups

Variables	Notsurvivinggroup n=31	Survivorgroup n=49	pvalue
Age, years	69±14	66±12	0.31
Gender, male	19(61%)	24(49%)	0.28
Hypertension	17(55%)	16(39%)	0.16
Diabetesmellitus	16(52%)	24(49%)	0.82
CAD	25(81%)	33(67%)	0.19
CABG	9(29%)	10(20%)	0.19
Hyperlipidemia	4(13%)	6(12%)	0.93
Ral in thelungs	28(93%)	41(85%)	0.28
Pretibialedema	27(87%)	28(57%)	**0.005**
Systolicbloodpressure, mmHg	108±18	117±17	0.02
Diastolicbloodpressure, mmHg	65±6	70±9	0.02

Abbreviations : CABG; Coronary artery bypass grafting , CAD; Coronary artery disease. Mean ± SD for numerical variables, frequencies (%) for categorical variables.

Table II: Laboratory data of groups

Parameters	notsurvivinggroup n=31	survivorgroup n=49	pvalue
Hemoglobin (g/dL)	11.49±2.09	11.64±1.85	0.73
Hematocrit (%)	36.78±6.26	37.18±5.56	0.77
Lymphocyte (NULL)	1.39±0.67	1.79±0.92	0.04
Urea (mg/dL)	101±46	67±40	<0.01
Creatinine (mg/dL)	1.65±0.53	1.15±0.38	<0.01
Albumin (gr/dL)	2.49±0.36	3.11±0.43	<0.01
Creatinine-albuminratio	0.68±0.27	0.38±0.18	<0.01
CRP(mg/dL)	2.09±1.54	1.49±1.43	0.08
ALT(U/L)	25.19±24.14	26.73±17.79	0.74
AST(U/L)	33.32±30.03	33.47±18.57	0.97
Total protein(g/dL)	6.77±0.61	6.74±0.76	0.87
Glucose(mg/dL)	171.26±110.25	167.45±98.39	0.87
HDL cholesterol(mg/dL)	30.26±11.24	35.96±18.97	0.14
LDL cholesterol (mg/dL)	80.42±23.84	87.69±28.29	0.24
Total cholesterol(mg/dL)	140.35±34.07	147.50±39.82	0.41
Triglyceride (mg/dL)	121.19±104.64	115.24±52.11	0.74
Na (mmol/L)	133.55±5.05	135.55±4.50	0.07

Abbreviations : ALT; Alanine aminotransferase, AST; Aspartate aminotransferase, CRP; C- reactive protein, HDL; High-Density Lipoprotein, LDL; Low-Density Lipoprotein, Na; Sodium.Mean ± SD for numerical variables.

In relation to the findings from transthoracic echocardiography, no statistically significant distinctions were noted between the two groups regarding IVS (p=0.81), PW (p=0.23), LVDD (p=0.25), LVDS (p=0.34), LA (p=0.18), RV (p=0.31), and RA (p=0.26) values. However, the deceased HF group had a statistically lower LVEF value (p=0.04). There was no statistically significant difference between the non-survivor and survivor groups in terms of electrocardiographic features such as sinus rhythm (p= 0.44, 15% vs. 28%, respectively) and atrial fibrillation (p= 0.70, 14% vs. 20%, respectively) (Table III). Moreover, there were no notable variances in medication utilization among the patients under study, with no statistically significant differences observed between the two groups (p > 0.05) (Table IV). The sensitivity and specificity of one-year mortality in HF patients with a creatinine-albumin ratio cut-off of 0.45 were 81% and 78%, respectively (Figure 1).

Table III: Echocardiography and electrocardiography parameters of the groups

Parameters	notsurvivinggroup n=31	survivorgroup n=49	pvalue
IVS (cm)	1.12±0.16	1.11±0.17	0.81
PW(cm)	2.58±6.81	1.09±0.20	0.23
LVDD (cm)	7.70±0.56	5.70±0.72	0.25
LVSD (cm)	4.85±1.04	4.51±0.90	0.34
LA (cm)	4.80±0.73	4.59±0.59	0.18
RV (cm)	4.28±0.75	4.05±0.79	0.31
RA (cm)	4.80±0.90	4.60±0.65	0.26
LVEF (%)	29.48±7.44	32.69±6.47	0.04
Sinusrhythm	15(48.3%)	28(57.1%)	0.44
Atrialfibrillation	14(45.1%)	20(40.8%)	0.70

Abbreviations : IVS; Interventricular septum, LA; Left atrium, LVDD; Left ventricular end-diastolic diameter, LVDS; Left ventricular end-systolic diameter, LVEF; Left ventricular ejection fraction, PW; Posterior wall, RA; Right atrium, RV; Right ventricle. Mean ± SD for numerical variables, frequencies (%) for categorical variables.

Table IV: Information on medicines usage

Parameters	notsurvivinggroup n=31	survivorgroup n=49	pvalue
ACE inhibitor	21(68%)	41(85%)	0.06
Beta-blocker	29(93%)	44(90%)	0.56
CCB	3(10%)	6(12%)	0.72
ASA	21(68%)	33(67%)	0.97
Diuretic	29(93%)	41(84%)	0.19
Digoxin	5(16%)	12(25%)	0.37
Spironolactone	16(52%)	25(51%)	0.96
Nitrate	2(7%)	4(8%)	0.78
Oral anticoagulant	10(32%)	12(24%)	0.45

Abbreviations : ACEI; Angiotensin converting enzyme inhibitor, ,ASA; Acetyl salicylic acid, CCB; Calcium channel blocker. Frequencies (%) for categorical variables.

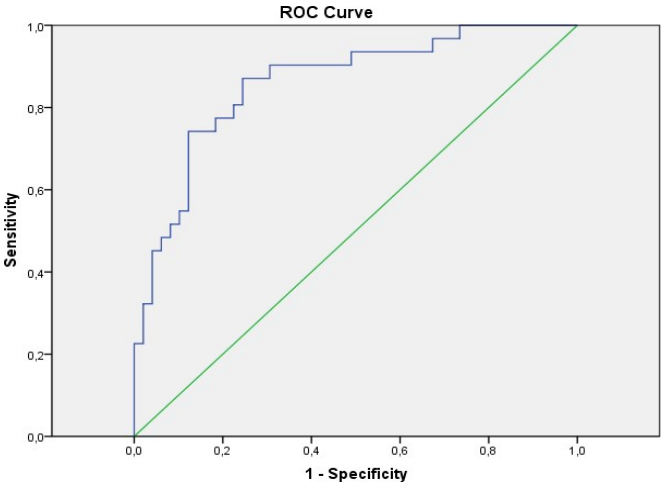

Figure 1. Representation of 1-year mortality due to all causes by serum creatinine-albumin ROC analysis in heart failure

DISCUSSION

Our study demonstrates that elevated creatinine levels and low albumin levels are frequently observed in patients admitted to the hospital due to acute decompensated systolic HF. Furthermore, we found that the creatinine-to-albumin ratio at the time of admission is associated with all-cause mortality within one year after discharge.

HF, which develops at the core of diseases such as coronary artery disease and hypertension and increases in prevalence with aging, remains a significant cause of morbidity and mortality in society[12]. It is emphasized that HF patients are frequently hospitalized within the past year and have high 5-year mortality rates despite treatment. In this study, the one-year mortality rate due to all causes was observed to be 39%. Factors such as advances in medical methods, treatments, and increased life expectancy have been identified as contributing to the increased prevalence of HF, making it a threatening condition to public health. Identifying high-risk individuals among HF patients and predicting mortality risk are crucial for their management. In this context, various parameters such as low LVEF, age, diabetes, renal insufficiency, low albumin, high-sensitivity C-reactive protein, low serum sodium, low hemoglobin level, and low body mass index have been used to predict high-risk HF patients[7,8,13] with increased mortality risk in chronic HF patients, there is insufficient data in the context of acute decompensated HF[14]. This study took a different approach by including only patients with systolic HF and LVEF ≤ 40% in the study group. Within this framework, the study established a notable correlation between elevated creatinine levels, low albumin levels, and reduced LVEF with increased mortality risk. Another similar study conducted in 2014 with similar characteristics also found a relationship between reduced albumin levels and mortality risk in patients with acute decompensated HF[15]. Similarly, this study also showed an association between low albumin levels, elevated creatinine levels, and reduced lymphocyte count with increased mortality risk. Yet, due to the relatively limited sample size in this study, it's possible that certain statistically significant variances might have gone undetected.

Hypoalbuminemia is frequently observed in HF patients, but it is noted that there is not enough epidemiological research in this regard[16,17]. Studies have reported that albumin deficiency is observed in 18% to 89% of HF patients[18]. For instance, in the CHARM study that included 2679 systolic and diastolic HF patients, the prevalence of hypoalbuminemia was determined as 18%[16]. In another study, the prevalence of hypoalbuminemia was found to be 25% in 1726 patients[17]. However, this study observed a prevalence of 81% for albumin deficiency. This high prevalence is attributed to the potential influence of excessive volume load on albumin deficiency among the patients enrolled in the study.

Albumin, the most abundant plasma protein in the body with a weight of 65 kDa, is synthesized, degraded, and distributed based on various factors. Factors such as malnutrition, inadequate production of liver enzymes,

cachexia, chronic inflammation, increased catabolism, hemodilution, protein-losing enteropathy, and nephrotic syndrome can contribute to albumin deficiency. Particularly in decompensated HF patients, hemodilution due to excessive volume load is considered one of the main reasons for albumin deficiency[19].

Kidney dysfunction is common in HF patients and is associated with mortality[20]. For instance, an analysis of 1407 HF patients demonstrated that serum creatinine level is an independent predictor for both 30-day and 1-year mortality[21]. In the same vein, this study revealed a pronounced correlation between elevated creatinine levels and mortality among patients who had deceased. However, this study only examined 1-year mortality. The association of low systolic and diastolic blood pressure with mortality has been emphasized, and comparable results have been noted in other investigations where low systolic and diastolic blood pressure were linked to elevated mortality in HF patients[22]. Low serum sodium levels have also been associated with increased mortality, especially in decompensated HF patients. Anemia has been highlighted as an independent risk factor in decompensated HF patients. The research also noted anemia in 58% of patients. However, despite observing lower hemoglobin levels in the deceased patient group, no statistically significant difference was detected. This result was attributed to the limited number of patients, which could make such analysis challenging. Overall, the study examined parameters that could predict high mortality risk in HF patients and highlighted factors like low albumin levels, elevated creatinine levels, and low lymphocyte counts as associated with increased mortality. However, it was noted that larger and more comprehensive studies are needed.

In this study, the association between increased mortality and factors such as low albumin, total cholesterol, hemoglobin, and lymphocyte count was established. Similarly, the analysis in this study revealed an association between elevated creatinine levels, low systolic blood pressure, and elevated urea levels with increased mortality. This phenomenon can be explained by the adverse effects of factors like reduced cardiac output, renal perfusion impairment, hypertension, and diabetes on the heart and kidneys. Additionally, low serum sodium levels were noted to be associated with increased mortality in decompensated HF patients[23]. Similar observations in different studies have shown that low serum sodium levels increase short and long-term mortality risk. Nevertheless, owing to the restricted patient sample size in this study, low serum sodium levels did not reach statistical significance[24]. It is noted that anemia is also an independent risk factor in decompensated HF patients. Previous studies have indicated that anemia in chronic HF patients increases hospitalization and mortality risk[25]. In this study, 58% of the patients had anemia, but despite lower hemoglobin levels in the deceased patient group, no statistically significant difference was found. This was ascribed to the limited patient cohort included in the study.

Limitations

The constraints of this study are manifold. Primarily, the relatively small size of the patient cohort may limit the applicability of the results. Additionally, crucial factors such as dietary habits and exercise patterns were not accounted for, potentially confounding the results. The exploration of variables like malnutrition was also inadequate. The retrospective design introduces uncertainty in establishing causal relationships definitively. Furthermore, relying on data from a single center may limit the extrapolation of findings to other healthcare settings. The follow-up period of only one year might not suffice to fully understand the long-term implications of the results. Moreover, the study primarily focused

on the initial creatinine-albumin value, neglecting other potentially influential variables. These limitations underscore the need for more comprehensive investigations to enhance the robustness and applicability of the findings.

CONCLUSION

Our research revealed an association between one-year, all-cause mortality in patients with systolic decompensated HF and decreased albumin levels, elevated creatinine levels, and an increased creatinine-to-albumin ratio. These findings suggest that the creatinine-to-albumin ratio may serve as a valuable prognostic indicator for these patients, providing insights without additional costs. However, larger randomized controlled trials are needed to validate these findings conclusively.

Ethics Committee Approval: The research received approval from the Dicle University Ethics Committee (dated 27 November 2015, numbered 221) and consisted of individuals admitted to the hospital with a diagnosis of HF.

Conflict of Interest: The authors declared no conflicts of interest.

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