

■ Research Article

Lactate levels as a predictor of mortality in patients with diabetic ketoacidosis in the emergency department

Acil serviste diyabetik ketoasidozda mortalite prediktörü olarak laktat düzeyleri

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Abstract

Aim: Diabetic ketoacidosis (DKA) is a life-threatening metabolic disorder commonly seen in patients with diabetes, particularly in emergency departments. Early identification of high-risk patients is crucial for reducing mortality. Lactate, a marker of tissue hypoxia, may have prognostic value in predicting outcomes in DKA patients.

Material and Methods: This retrospective study included patients diagnosed with DKA in the emergency department of a tertiary healthcare center between January 1, 2019, and January 1, 2024. Patients were identified using the hospital's electronic medical records system. Data collected included demographic characteristics, clinical parameters, laboratory results, and patient outcomes. The diagnosis of DKA was based on established clinical and laboratory criteria, including hyperglycemia, metabolic acidosis, and ketonemia or ketonuria. The primary outcome was in-hospital mortality.

Results: A total of 85 patients were included in the study, with a mean age of 54 years (IQR: 35–70). Of the study population, 44.7% were female. The overall mortality rate was 15.3%, with 72 patients surviving (84.7%) and 13 patients not surviving (15.3%). The median age of non-survivors was significantly higher than that of survivors (66 years vs. 51 years, $p = 0.049$). Additionally, lactate levels were significantly higher in non-survivors than in survivors, indicating a potential prognostic role of lactate in predicting outcomes in DKA patients.

Conclusion: Elevated lactate levels at admission are strongly associated with increased mortality in patients with diabetic ketoacidosis. Monitoring lactate levels in the emergency department could be a useful prognostic tool for identifying high-risk patients and guiding early interventions.

Keywords: Diabetic ketoacidosis, lactate, mortality

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Öz

Amaç: Diyabetik ketoasidoz (DKA), özellikle acil servislerde diyabet hastalarında yaygın olarak görülen, hayatı tehdit eden metabolik bir bozukluktur. Yüksek riskli hastaların erken tespiti, mortalitenin azaltılması açısından kritik öneme sahiptir. Doku hipoksisinin bir belirteci olan laktat, DKA hastalarında sonuçları öngörmede prognostik değere sahip olabilir.

Gereç ve Yöntemler: Bu retrospektif çalışmaya, 1 Ocak 2019 - 1 Ocak 2024 tarihleri arasında üçüncü basamak bir sağlık merkezinin acil servisinde DKA tanısı alan hastalar dahil edilmiştir. Hastalar, hastanenin elektronik tıbbi kayıt sistemi kullanılarak belirlenmiştir. Toplanan veriler arasında demografik özellikler, klinik parametreler, laboratuvar sonuçları ve hasta sonuçları yer almıştır. DKA tanısı, hiperglisemi, metabolik asidoz ve ketonemi veya ketonüriyi içeren yerleşik klinik ve laboratuvar kriterlere dayanarak konulmuştur. Birincil sonuç ölçütü hastane içi mortalite olarak belirlenmiştir.

Bulgular: Çalışmaya toplam 85 hasta dahil edilmiştir ve hastaların ortalama yaşı 54 yıl (IQR: 35–70) olarak bulunmuştur. Çalışma popülasyonunun %44,7'si kadındı. Genel mortalite oranı %15,3 olup, 72 hasta (%84,7) sağ kalırken, 13 hasta (%15,3) hayatını kaybetmiştir. Hayatta kalamayan hastaların medyan yaşı, sağ kalanlara kıyasla anlamlı derecede daha yüksekti (66 yıl vs. 51 yıl, $p = 0,049$). Ayrıca, laktat seviyeleri hayatta kalamayan hastalarda sağ kalanlara kıyasla anlamlı derecede daha yüksekti ve bu durum, laktatın DKA hastalarındaki sonuçları öngörmede potansiyel bir prognostik role sahip olabileceğini göstermektedir.

Sonuç: Başvuru anındaki yüksek laktat seviyeleri, diyabetik ketoasidoz hastalarında artmış mortalite ile güçlü bir şekilde ilişkilidir. Acil serviste laktat seviyelerinin izlenmesi, yüksek riskli hastaların belirlenmesi ve erken müdahalelerin yönlendirilmesi için faydalı bir prognostik araç olabilir.

Anahtar Kelimeler: Diyabetik ketoasidoz, laktat, mortalite.

Introduction

Diabetic ketoacidosis (DKA) is a serious metabolic complication characterized by hyperglycemia, ketosis, and metabolic acidosis, commonly seen in patients with type 1 diabetes (1-3). This condition develops due to insulin deficiency and the effects of increased counter-regulatory hormones (glucagon, cortisol, adrenaline). Frequently encountered in emergency departments, DKA can lead to increased mortality and morbidity rates if not treated promptly and appropriately (4,5). Given the severity and potential complications of DKA, timely recognition and management in emergency settings are of critical importance.

Early diagnosis and rapid intervention in DKA significantly impact both short- and long-term outcomes. Early identification reduces the need for intensive care and helps prevent complications. It is crucial for emergency physicians to quickly recognize DKA and initiate appropriate treatment, as this directly affects patient prognosis and the efficiency of healthcare delivery. Since the symptomatology of DKA can sometimes be nonspecific, there is a need for rapid diagnostic tools. In this context, the evaluation of biochemical parameters plays a vital role, particularly in the early stages of clinical management (6,7).

Lactate levels are used as a prognostic marker in various

acute clinical conditions and play a crucial role in assessing the severity of metabolic acidosis. In DKA, elevated lactate levels are considered an indicator of hypoperfusion and tissue hypoxia. There is increasing evidence in the literature that lactate has a significant impact on the prognosis of DKA. Studies have reported higher mortality rates in patients with elevated lactate levels (8,9). Therefore, lactate is thought to be a valuable prognostic marker for risk assessment in DKA patients in the emergency department.

The aim of this study is to examine the relationship between lactate levels and mortality in patients diagnosed with DKA in the emergency department.

Material and Methods

This study was conducted with the approval of the Taksim Education and Research Hospital's Ethics Committee (Date: 30.10.2024, Decision No: 13). The study adhered to the ethical principles outlined in the Declaration of Helsinki. This retrospective study was carried out on patients diagnosed with DKA in the emergency department of a tertiary healthcare facility between January 1, 2019, and January 1, 2024. Due to the retrospective nature of the study, informed consent was not obtained from the patients, and exemption was granted by the ethics committee.

All patients aged 18 and over who were diagnosed with DKA were included in the study. Patients who received diagnoses other than DKA upon admission, those whose DKA diagnosis could not be confirmed due to incomplete data, and patients with other serious clinical conditions such as renal failure or sepsis were excluded from the study.

The following data were collected by reviewing the patients' medical records: age, gender, blood pressure (systolic and diastolic), pulse, respiratory rate, Glasgow Coma Scale (GCS) score, oxygen saturation (SPO₂), blood glucose, creatinine, blood urea nitrogen (BUN), albumin, C-reactive protein (CRP), pH, partial pressure of carbon dioxide (pCO₂), bicarbonate (HCO₃), and lactate levels. Additionally, hospital length of stay and in-hospital mortality were recorded. Blood gas laboratory values were measured using the ABL800 FLEX blood gas analyzer (Radiometer).

The diagnosis of DKA was based on the patient's clinical findings and laboratory results. Diagnostic criteria included hyperglycemia (blood glucose level >250 mg/dL), metabolic acidosis (pH <7.3), low serum bicarbonate levels (<15 mmol/L), and either ketonuria or ketonemia (10). The primary outcome of the study was in-hospital mortality.

Statistical Analysis

All statistical analyses were conducted using IBM SPSS Statistics for Windows, version 29.0 (IBM Corp., Armonk, NY, USA) and MedCalc version 20.104 (MedCalc Software Ltd., Ostend, Belgium). Descriptive statistics were calculated for each variable, with continuous variables presented as medians with interquartile ranges (IQR) or means \pm standard deviation (SD), based on normality testing. Categorical variables were summarized using frequencies and percentages. Data normality was assessed through histograms and the Shapiro-Wilk test. Group comparisons were made using the Student's t-test for continuous variables with normal distribution and the Mann-Whitney U test for non-normal distributions. Categorical variables were compared using the Chi-square test or Fisher's exact test, as appropriate.

The diagnostic accuracy of lactate levels for predicting in-hospital mortality was evaluated using receiver operating characteristic (ROC) curve analysis, with the area under the ROC curve (AUROC) computed. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated at the optimal cutoff identified by Youden's Index (11). A p-value of <0.05 was considered statistically significant.

Results

A total of 85 patients with diabetic ketoacidosis were included in the study. Of these, 72 (84.7%) survived, while 13 (15.3%) did not survive. Female patients comprised 44.7% of the total population, with no statistically significant difference in the proportion of females between survivors (41.7%, n=30) and non-survivors (61.5%, n=8) (p = 0.185). The median age was significantly higher among non-survivors [66 years, IQR 49 - 81] than survivors [51 years, IQR 33.5 - 67.5] (p = 0.049).

Systolic blood pressure (BP) was lower in non-survivors [111 \pm 30.3 mmHg] compared to survivors [124 \pm 24.3 mmHg], but this difference was not statistically significant (p = 0.087). Similarly, diastolic BP was lower in non-survivors [66.4 \pm 16.8 mmHg] than in survivors [74.8 \pm 16.6 mmHg], without a significant difference (p = 0.096). The heart rate was higher in non-survivors [107 \pm 24.7 bpm] than in survivors [98.8 \pm 19.2 bpm], though this difference was also not statistically significant (p = 0.199).

The respiratory rate was higher among non-survivors [22 breaths/min, IQR 16 - 32] compared to survivors [19 breaths/min, IQR 15 - 25], but this difference did not reach statistical significance (p = 0.163). Non-survivors had significantly lower Glasgow Coma Scale (GCS) scores [14, IQR 12 - 15] compared to survivors who had a median score of 15 (p = 0.002). Oxygen saturation (SPO₂) levels were significantly lower among non-survivors [95%, IQR 90 - 96] compared to survivors [98%, IQR 96 - 99] (p = 0.016).

Glucose levels did not differ significantly between non-survivors [634 \pm 263 mg/dL] and survivors [595 \pm 188 mg/dL] (p = 0.518). Creatinine levels were higher in non-survivors [1.69 mg/dL, IQR 1.12 - 2.05] compared to survivors [1.27 mg/dL, IQR 1.00 - 1.74], although this difference was not statistically significant (p = 0.269). Blood urea nitrogen (BUN) levels were also elevated among non-survivors [50 mg/dL, IQR 22 - 68] compared to survivors [25 mg/dL, IQR 17 - 47], with no statistically significant difference (p = 0.166).

Albumin levels were lower in non-survivors [34.5 \pm 13.7 g/dL] than in survivors [40 \pm 8.58 g/dL], but the difference was not statistically significant (p = 0.058). C-Reactive Protein (CRP) levels were higher among non-survivors [115 mg/L, IQR 31 - 171] compared to survivors [25 mg/L, IQR 4.8 - 129], though this difference did not reach statistical significance (p = 0.092).

The pH level did not differ significantly between survivors and non-survivors (p = 0.893). Levels of partial pressure of carbon dioxide (pCO₂) were similar between the two groups (p = 0.881). Bicarbonate (HCO₃) levels were lower in non-survivors [11.8 mmol/L, IQR 8.4 - 17.5] compared to survivors [12.6 mmol/L, IQR 9.38 - 16.7], but this difference was not statistically significant (p = 0.826).

Lactate levels were significantly higher among non-survivors [5.25±0.88 mmol/L] compared to survivors [2.95±1.47 mmol/L], with a mean difference of 2.3 mmol/L (95% CI: 1.46-3.14, p<0.001). When comparing patients with low lactate (≤ 3.5 mmol/L, n=25) to those with high lactate (> 3.5 mmol/L, n=60), older age was observed in the high lactate group [59.5 years, IQR 41.8 - 73] versus the low lactate group [37 years, IQR 30 - 56] (p = 0.007). Heart rate was higher in the high lactate group [103±20.5 bpm] than in the low lactate group [92.1±17.4 bpm] (p = 0.02). Respiratory rates were significantly higher in patients with elevated lactate [20.5 breaths/min, IQR 16 - 29.3] compared to those with low lactate [16 breaths/min, IQR 14 - 20] (p = 0.013). (Tables 1 2,3).

The mortality rate was significantly higher in patients with high lactate levels (21.7%) compared to those with low lactate levels (0%) (p = 0.009).

The diagnostic performance of lactate levels for predicting in-hospital mortality in patients with DKA yielded an Area Under the Receiver Operating Characteristic Curve (AUROC) of 0.91 (95% CI: 0.85 - 0.96) (Figure 1). Using a lactate cutoff of > 3.5 mmol/L, the sensitivity was 87% (95% CI: 70% - 96%)

and specificity was 85% (95% CI: 76% - 92%), with a positive predictive value (PPV) of 67% (95% CI: 54% - 78%) and a negative predictive value (NPV) of 95% (95% CI: 88% - 98%).

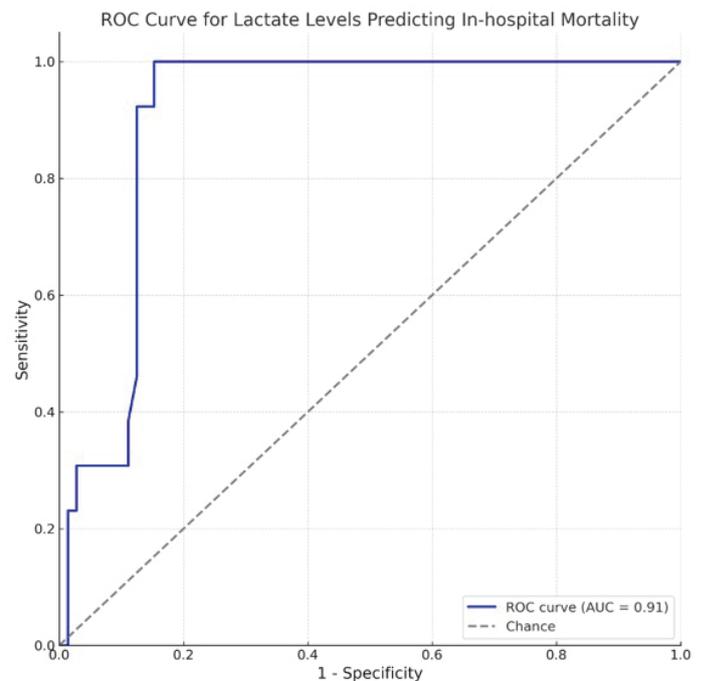


Figure 1. Receiver Operating Characteristic Curve for Lactate Levels in Predicting In-hospital Mortality in Patients with Diabetic Ketoacidosis

Table 1. Baseline Characteristics and Outcomes of Patients with Diabetic Ketoacidosis by Survival Status.

Variable	All (n=85)	Survivor (n=72)	Deceased (n=13)	p	Mean Difference (95% CI)
Sex (Female)	38 (44.7%)	30 (41.7%)	8 (61.5%)	0.185	-
Age (years)	54 (35 - 70)	51 (33.5 - 67.5)	66 (49 - 81)	0.049	-
Systolic BP (mmHg)	122±25.5	124±24.3	111±30.3	0.087	-
Diastolic BP (mmHg)	73.5±16.8	74.8±16.6	66.4±16.8	0.096	-
Heart Rate (bpm)	100±20.2	98.8±19.2	107±24.7	0.199	-
Respiratory Rate (/min)	20 (15 - 28)	19 (15 - 25)	22 (16 - 32)	0.163	-
GCS,	15 (15 - 15)	15 (15 - 15)	14 (12 - 15)	0.002	-
SPO2 (%)	97 (95 - 99)	98 (96 - 99)	95 (90 - 96)	0.016	-
Glucose (mg/dL)	601±200	595±188	634±263	0.518	-
Creatinine (mg/dL)	1.29 (1.00 - 1.81)	1.27 (1.00 - 1.74)	1.69 (1.12 - 2.05)	0.269	-
BUN (mg/dL)	26 (17 - 50)	25 (17 - 47)	50 (22 - 68)	0.166	-
Albumin (g/dL)	39.2±9.64	40±8.58	34.5±13.7	0.058	-
CRP (mg/L)	36 (5 - 131)	25 (4.8 - 129)	115 (31 - 171)	0.092	-
pH	7.18 (7.09 - 7.29)	7.19 (7.11 - 7.29)	7.17 (7.07 - 7.30)	0.893	-
pCO2 (mmHg)	31.8±9.69	31.9±9.95	31.4±8.43	0.881	-
HCO3 (mmol/L)	12.4 (9.3 - 17.1)	12.6 (9.38 - 16.7)	11.8 (8.4 - 17.5)	0.826	-
Lactate (mmol/L)	3.3±1.62	2.95±1.47	5.25±0.88	<0.001	2.3 (1.46 - 3.14)

Abbrev. : BP: Blood Pressure;bpm: Beats per Minute; GCS: Glasgow Coma Scale; SPO2: Oxygen Saturation; BUN: Blood Urea Nitrogen; CRP: C-Reactive Protein; pCO2: Partial Pressure of Carbon Dioxide; HCO3: Bicarbonate.

Table 2. Comparison of Baseline Characteristics and Outcomes in Patients with Low vs. High Lactate Levels.

Variable	Low Lactate (n=25)	High Lactate (n=60)	p	Mean Difference (95% CI)
Sex(Female)	11 (44%)	27 (45%)	0.933	-
Age (years)	37 (30 - 56)	59.5 (41.8 - 73)	0.007	-
Systolic BP (mmHg)	121±19.9	122±27.7	0.950	-
Diastolic BP (mmHg)	72.3±12.1	74±18.5	0.661	-
Heart Rate (bpm)	92.1±17.4	103±20.5	0.02	11.1 (1.81 - 20.4)
Respiratory Rate (/min)	16 (14 - 20)	20.5 (16 - 29.3)	0.013	-
GCS,	15 (15 - 15)	15 (14 - 15)	0.012	-
SPO2 (%)	98 (96 - 99)	97 (93.8 - 99)	0.243	-
Glucose (mg/dL)	558±150	619±216	0.205	-
Creatinine (mg/dL)	1.07 (0.9 - 1.47)	1.35 (1.04 - 1.81)	0.171	-
BUN (mg/dL)	21 (16 - 32)	28 (20 - 50.3)	0.137	-
Albumin (g/dL)	39.2±9.73	39.2±9.68	0.975	-
CRP (mg/L)	23 (5 - 102)	39.4 (5.75 - 147)	0.461	-
pH	7.26 (7.17 - 7.30)	7.17 (7.08 - 7.28)	0.053	-
pCO2 (mmHg)	31.5±9.55	31.9±9.82	0.841	-
HCO3 (mmol/L)	14 (10 - 18.3)	11.3 (9.25 - 16.6)	0.201	-
Mortality	0 (0%)	13 (21.7%)	0.009	-

Abbrev.: BP: Blood Pressure; bpm: Beats per Minute; GCS: Glasgow Coma Scale ;SPO2: Oxygen Saturation; BUN: Blood Urea Nitrogen; CRP: C-Reactive Protein; pCO2: Partial Pressure of Carbon Dioxide; HCO3: Bicarbonate.

Table 3. Diagnostic Performance of Lactate Levels for Predicting In-hospital Mortality in Patients with Diabetic Ketoacidosis.

Parameter	AUROC (95% CI)	p	Youden's Index (J)	Criterion	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Lactate Level	0.91 (0.85 - 0.96)	< 0.001	0.75	> 3.5 mmol/L	87% (70% - 96%)	85% (76% - 92%)	67% (54% - 78%)	95% (88% - 98%)

Abbrev.: AUROC: Area Under the Receiver Operating Characteristic Curve; CI: Confidence Interval; PPV: Positive Predictive Value; NPV: Negative Predictive Value; J: Youden's Index

Discussion

The main finding of this study is that lactate levels at the time of admission are significantly associated with in-hospital mortality in DKA patients. Mortality rates were considerably higher in patients with lactate levels above 3.5 mmol/L compared to those with lower levels. This finding suggests that lactate is a valuable marker for predicting clinical prognosis in DKA patients.

DKA is a common condition encountered in emergency departments and, if not treated promptly, can lead to severe outcomes. Initiating appropriate treatment quickly in patients diagnosed with DKA plays a crucial role in reducing both mortality and morbidity (12-14). Early recognition of the condition and timely initiation of treatment by emergency physicians significantly improve patient survival and shorten hospital stays. The clinical spectrum of DKA ranges from mild symptoms to severe complications, such as loss of consciousness and multiple organ failure, making the timely

and effective use of diagnostic tools critically important (15). In this context, carefully evaluating the biochemical parameters of patients upon admission is essential to initiating a rapid intervention process.

Lactate plays a significant role in the pathophysiology of DKA, and the results of this study support its importance as a critical marker in the progression of the disease. In DKA, insulin deficiency and the effects of counter-regulatory hormones increase gluconeogenesis and lipolysis, leading to elevated free fatty acids and the production of ketone bodies. While the accumulation of ketone bodies causes metabolic acidosis, hypoperfusion and tissue hypoxia contribute to the accumulation of lactate. Elevated lactate levels indicate a deficiency in tissue oxygenation and the activation of anaerobic metabolism (16). Therefore, elevated lactate is associated with poor prognosis in DKA patients and correlates with higher mortality rates.

In this study, high lactate levels at the time of admission were found to be associated with in-hospital mortality in DKA patients. Similarly, in the prospective cohort study by Suwanto et al., lactate levels of ≥ 4 mmol/L were identified as an independent predictor of five-day mortality (17). Likewise, Siregar et al. demonstrated in their 72-hour mortality prediction model that the risk of mortality increased fivefold in patients with lactate levels above 4 mmol/L (9). However, Cully et al., who examined pediatric DKA patients, found that while lactic acidosis was common in this patient group, it was not significantly associated with mortality (18). These findings support the prognostic value of lactate in adult DKA patients, although this relationship may not always apply to pediatric populations due to differing physiological responses.

Lactate elevation in DKA reflects underlying metabolic stress, which is often influenced by a variety of precipitating factors that may also affect patient outcomes. Precipitating factors for DKA, such as infections, acute coronary syndromes, and arrhythmias, are known to significantly impact clinical outcomes and are closely associated with both lactate elevation and mortality. These conditions exacerbate metabolic stress and hypoxia, contributing to the pathophysiological complexity of DKA. Previous studies have highlighted that infections, in particular, are a major contributor to lactic acidosis in critically ill patients, further underlining their relevance in this context (19). A more detailed exploration of these factors in future studies could provide valuable insights into their interplay with lactate levels and patient outcomes in DKA.

Lastly, current clinical guidelines for the management of diabetic ketoacidosis emphasize the importance of rapid assessment and correction of metabolic disturbances but do not consistently address the prognostic role of lactate levels. While lactate monitoring is well-established in other critical care settings, such as sepsis management, its routine use in DKA has not yet been widely adopted. The findings of this study suggest that elevated lactate levels at admission could serve as a valuable prognostic tool in DKA, aiding in the early identification of high-risk patients. By highlighting the prognostic significance of lactate, this study contributes to the growing body of evidence supporting its integration into clinical practice and may inform future updates to DKA management guidelines.

Limitations of the Study

This study has several limitations. First, its retrospective design limits the ability to establish a causal relationship between

elevated lactate levels and mortality in diabetic ketoacidosis (DKA). Second, the study was conducted at a single tertiary healthcare center, which may reduce the generalizability of the findings to other populations and settings. Additionally, certain confounding factors, such as the presence of comorbid conditions or the variability in treatment approaches, may have influenced the outcomes. Moreover the absence of a control group, such as patients without lactate elevation but with other factors contributing to mortality, limits the generalizability of our findings. Future prospective studies incorporating control groups are needed to enhance the robustness and comparability of results. Lastly, the sample size, particularly in the non-survivor group, was relatively small, which could affect the statistical power of the study.

In conclusion, elevated lactate levels at the time of admission are significantly associated with increased in-hospital mortality in patients presenting with diabetic ketoacidosis in the emergency department. Monitoring lactate levels may serve as a valuable prognostic tool in the early identification of high-risk patients, enabling prompt and appropriate interventions.

Ethical Approval

This study was approved by the Taksim Education and Research Hospital's ethics committee (ethics committee ruling number: 13, date: 30.10.2024).

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Conflicts of Interest

Authors declare that they have no conflicts of interest.

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