Section: Medicine

Systematic Review Article

FLUID RESUSCITATION STRATEGIES IN ACUTE PANCREATITIS: A SYSTEMATIC REVIEW

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ABSTRACT

Background: Acute pancreatitis (AP) is a common gastrointestinal emergency with clinical severity ranging from mild, self-limiting disease to severe pancreatitis associated with organ failure and increased mortality. Early fluid resuscitation is a cornerstone of management, aiming to restore intravascular volume, improve pancreatic perfusion, and reduce complications. However, the optimal fluid resuscitation strategy, including the type, volume, rate, and timing of fluid administration, remains controversial. While aggressive hydration was traditionally recommended, recent evidence supports a more individualized, goal-directed approach to minimize the risk of fluid overload and related complications. Therefore, this systematic review aims to evaluate the current evidence on fluid resuscitation strategies and their effects on clinical outcomes in patients with acute pancreatitis. The objective is to compare the effectiveness and safety of different fluid resuscitation strategies and intravenous fluid types in acute pancreatitis, and to assess their impact on disease severity, organ failure, pancreatic necrosis, length of hospital stay, mortality, and fluid-related adverse events.

Materials and Methods: This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A comprehensive literature search was performed in PubMed, Scopus, Web of Science, Embase, and the Cochrane Library using relevant keywords acute pancreatitis, fluid resuscitation, fluid resuscitation strategies and clinical outcome. Article published from year 2002 included. Eligible studies were screened independently by two reviewers based on predefined inclusion and exclusion criteria. Data on study characteristics, fluid resuscitation strategies, disease severity, organ failure, pancreatic necrosis, length of hospital stay, mortality, and fluid-related adverse events were extracted using a standardized data collection form. The methodological quality of the included studies was assessed using appropriate risk-of-bias tools, and the findings were synthesized qualitatively.

Results: Evidence suggests that early, individualized fluid resuscitation improves outcomes in acute pancreatitis. Lactated Ringer's solution generally reduced systemic inflammatory response syndrome (SIRS) and C-reactive protein (CRP) more effectively than normal saline. However, excessive fluid administration (>4.1 L/24 h) and rapid hemodilution were associated with increased organ failure, sepsis, and mortality. Hydroxyethyl starch (HES) and adjunctive therapies showed limited or inconsistent clinical benefits. Overall, early, goal-directed fluid therapy with preference for Lactated Ringer's solution while avoiding fluid overload appears most appropriate.

Conclusion: Early, individualized fluid resuscitation, particularly with Lactated Ringer's solution, may improve inflammatory outcomes in acute pancreatitis. However, excessive or rapid fluid administration may worsen complications. Further high-quality randomized trials are needed to define optimal fluid strategies and clarify the role of adjunctive therapies.

Keywords: acute pancreatitis, fluid resuscitation, fluid resuscitation strategies, clinical outcome

INTRODUCTION

Acute pancreatitis (AP) is a common gastrointestinal emergency and a major cause of hospitalization worldwide. Its clinical presentation ranges from mild, self-limiting inflammation to severe disease characterized by pancreatic necrosis, organ failure, and increased mortality. Early identification and appropriate management are essential to prevent disease progression and improve patient outcomes.

Fluid resuscitation is the cornerstone of early treatment in acute pancreatitis, aiming to restore intravascular volume, improve pancreatic perfusion, and prevent complications resulting from hypovolemia and systemic inflammation. However, the optimal fluid resuscitation strategy remains uncertain. While aggressive hydration was traditionally recommended, recent evidence suggests that excessive fluid administration may increase the risk of fluid overload, respiratory complications, and abdominal compartment syndrome. Consequently, current guidelines increasingly favor individualized, goal-directed fluid therapy using balanced crystalloids, particularly Lactated Ringer's solution, when appropriate.

Compared with Normal Saline (NS), Lactated Ringer's (LR) significantly reduced the risk of moderately severe/severe acute pancreatitis (Odds Ratio [OR] 0.49; 95% Confidence Interval [CI] 0.25–0.97), ICU admission (OR 0.33; 95% CI 0.13–0.81), and local complications (OR 0.42; 95% CI 0.20–0.88), with no significant differences in SIRS, organ failure, or hospital stay (Zhou S et al.,2021).[1]

Fluid therapy remains a fundamental component of early acute pancreatitis management; however, the supporting clinical evidence is limited and generally of low quality (Haydock MD et al., 2013).[2]

Aggarwal A et al. (2014) concluded that while early fluid resuscitation is fundamental in acute pancreatitis, the optimal type, rate, and volume of fluid therapy remain uncertain, highlighting the need for evidence-based fluid management strategies.[3]

Li XW et al. (2023) analyzed 9 Randomized Controlled Trials (RCTs) (953 patients) and found that aggressive intravenous hydration increased mortality in severe acute pancreatitis (Risk Ratio [RR] 2.45; 95% CI 1.37–4.40) and fluid-related complications in both severe and non-severe disease, supporting conservative fluid resuscitation.[4]

Despite numerous clinical trials and updated recommendations, there is ongoing debate regarding the ideal type, volume, rate, and timing of fluid administration in acute pancreatitis. Therefore, this systematic review aims to evaluate the current evidence on fluid resuscitation strategies and their impact on clinical outcomes, including disease severity, organ failure, complications, length of hospital stay, and mortality, to support evidence-based management of patients with acute pancreatitis.

Objectives: To compare the efficacy and safety of various fluid resuscitation strategies and intravenous fluid types in the management of acute pancreatitis, and to evaluate their effects on disease severity, organ failure, pancreatic necrosis, length of hospital stay, mortality, and fluid-related adverse events.

MATERIALS AND METHODS

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A comprehensive literature search was performed in PubMed, Scopus, Web of Science, Embase, and the Cochrane Library using relevant key words acute pancreatitis, fluid resuscitation, fluid resuscitation strategies and clinical outcome. Article published from year 2002 included. Original research studies including, case-control studies, longitudinal studies, cohort studies, randomized controlled trials, observational studies, case study evaluating fluid resuscitation strategies in acute pancreatitis included. Studies not reporting relevant outcomes, lacking extractable data, editorials, conference abstracts were excluded. Titles, abstracts, and full-text articles were independently screened by two reviewers, with disagreements resolved through discussion. Data extraction and quality assessment were performed independently using standardized tools appropriate for each study design. Due to heterogeneity in study designs and outcome reporting, the findings were synthesized narratively.

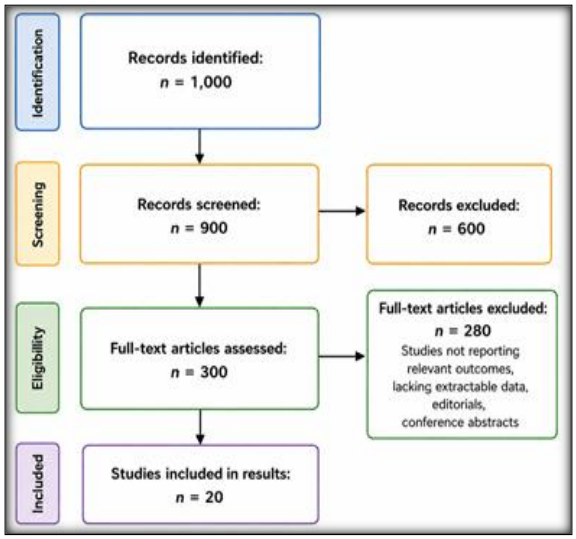


Figure: PRISMA Flow chart of Study Selection Process

RESULTS

A randomized controlled trial involving 40 patients with acute pancreatitis compared goal-directed and standard fluid resuscitation using either Lactated Ringer's solution (LR) or normal saline (NS). The mean fluid volume administered over 24 hours was similar between the goal-directed and standard

groups (4300 mL vs. 4600 mL; P = 0.87). Goal-directed therapy did not significantly reduce the incidence of systemic inflammatory response syndrome (SIRS) (11.8% vs. 13.0%; P = 0.85) or C-reactive protein (CRP) levels after 24 hours (87.1 vs. 69.2 mg/dL; P = 0.75) compared with standard resuscitation. In contrast, patients receiving Lactated Ringer's solution demonstrated a significantly greater reduction in SIRS (84% vs. 0%; P = 0.035) and lower CRP levels (51.5 vs. 104 mg/dL; P = 0.02) than those receiving normal saline, suggesting that LR is more effective in reducing systemic inflammation in acute pancreatitis (Wu BU et al., 2011).[5]

de-Madaria E et al. (2018) conducted a triple-blind, randomized controlled trial comparing Lactated Ringer's solution (LR) with normal saline (NS) in adults with acute pancreatitis (19 LR; 21 NS). At 48 hours, the median number of SIRS criteria was 1 (0–1) in the LR group versus 1 (1–2) in the NS group (p = 0.060). CRP levels were significantly lower with LR at 48 hours (28 [3–124] vs. 166 [78–281] mg/L; p = 0.037) and 72 hours (25 [3–169] vs. 217 [59–323] mg/L; p = 0.043). In vitro, LR inhibited macrophage inflammatory activation and Nuclear Factor Kappa B (NF-κB) signaling, supporting a direct anti-inflammatory effect of lactate. These findings suggest that Lactated Ringer's solution reduces systemic inflammation more effectively than normal saline in acute pancreatitis.[6]

Choosakul S et al. (2018) conducted a randomized controlled trial involving 47 patients with acute pancreatitis (24 received normal saline solution [NSS] and 23 received Lactated Ringer's solution [LRS]) using a goal-directed fluid resuscitation protocol. LRS was associated with a significantly greater reduction in SIRS at 24 hours (26.1% vs. 4.2%; P = 0.02), whereas SIRS at 48 hours was similar between the LRS and NSS groups (26.1% vs. 33.4%; P = 0.88). Mortality was 0% with LRS and 4.2% with NSS (P = 1.00). No significant differences were observed in CRP, Erythrocyte Sedimentation Rate (ESR), procalcitonin, local complications (21.7% vs. 29.2%; P = 0.74), or median hospital stay (6 vs. 5.5 days; P = 0.915). These findings suggest that LRS provides an early reduction in systemic inflammation during the first 24 hours, with no significant differences in later outcomes compared with NSS.[7]

Kayhan S et al. (2021) conducted a prospective randomized single-center study, 142 patients with acute pancreatitis received either Normal Saline Solution (NSS, n = 65) or Lactated Ringer's Solution (LRS, n = 77). The LRS group had a significantly lower incidence of moderate acute pancreatitis (p = 0.011), lower CRP levels at 48 hours (p = 0.010), and higher serum pH and bicarbonate levels (p < 0.001) than the NSS group, indicating reduced inflammation and disease severity with LRS.[8]

Lee A et al. (2021) conducted a double-blind randomized controlled trial involving 121 patients with acute pancreatitis, comparing Lactated Ringer's solution (LR) with Normal Saline (NS). Most participants had mild pancreatitis, and baseline SIRS prevalence was similar between the LR (27.9%) and NS (23.3%) groups. The primary outcome assessed changes in SIRS at 24 hours, with additional evaluation at 48 and 72 hours, disease severity, Intensive Care Unit (ICU) admission, hospital stay, and adverse events.[9]

Mao EQ et al. (2010) conducted a randomized study involving 115 patients with severe acute pancreatitis, comparing rapid (n = 56) and slow (n = 59) hemodilution. Rapid hemodilution was associated with a shorter time to sepsis (7.4 ± 1.9 vs. 10.2 ± 2.3 days), a higher 28-day sepsis incidence (78.6% vs. 57.6%), and lower in-hospital survival (66.1% vs. 84.7%, P < 0.05). The authors concluded that rapid hemodilution increased sepsis and mortality, recommending maintenance of hematocrit between 30% and 40% during the acute phase.[10]

Gardner TB et al. (2010) retrospectively evaluated 45 patients with severe acute pancreatitis, comparing early (≥33% of the 72-hour fluid volume administered within the first 24 hours; n = 17) and late (<33%; n = 28) fluid resuscitation. The late resuscitation group had significantly higher mortality (18% vs. 0%, p < 0.04) and a higher, though non-significant, rate of persistent organ failure (43% vs. 35%, p = 0.31). There was no difference in the total fluid volume administered over 72 hours.[11]

Brown A et al. (2002) evaluated 39 patients with acute pancreatitis, including 28 with necrotizing and 11 with interstitial pancreatitis. Patients with necrotizing pancreatitis presented earlier (18 vs. 38 hours, p = 0.005). Persistent hemoconcentration at 24 hours was observed only in patients with necrotizing pancreatitis (12/28 vs. 0/11, p = 0.009), despite similar fluid resuscitation volumes (4.0, 4.5, and 4.1 L, p = 0.81), suggesting that persistent hemoconcentration is associated with pancreatic necrosis.[12]

de-Madaria E et al. (2011) prospectively studied 247 patients with acute pancreatitis and found that receiving >4.1 L of fluid within the first 24 hours was independently associated with persistent organ failure, acute fluid collections, respiratory insufficiency, and renal insufficiency. In contrast, <3.1 L was not associated with organ failure, local complications, or mortality, while 3.1–4.1 L was associated with favorable outcomes.[13]

Warndorf MG et al. (2011) retrospectively studied 434 patients with acute pancreatitis and found that early fluid resuscitation reduced SIRS at 24 hr (15% vs 32%, P=0.001), 48 hr (14% vs 33%, P=0.001), and 72 hr (10% vs 23%, P=0.01), organ failure at 72 hr (5% vs 10%, P<0.05), ICU admission (6% vs 17%, P<0.001), and hospital stay (8 vs 11 days, P=0.01), with greater benefits in interstitial pancreatitis.[14]

Wall I et al. (2011) found that increased hydration in acute pancreatitis was associated with reduced pancreatic necrosis (15% vs 4%) and mortality (12% vs 3.5%, P=0.03). Hydration rates increased from 184 to 284 mL/hr during the first 6 hours and from 188 to 221 mL/hr during the first 12 hours (P=0.02),

suggesting improved outcomes with more aggressive fluid therapy.[15]

Kuwabara K et al. (2011) analyzed 9,489 adults with acute pancreatitis (AP) and found that 1.1% required ventilation, 1.7% hemodialysis, and 1.0% both. Higher fluid volume during the first 48 hours was associated with increased mortality in severe AP, whereas a higher Fluid Volume (FV) ratio, Total fluid volume given during the first 48 hours/ Fluid volume given during the first hour (FV48/FVH) was associated with lower mortality. The findings support severity-based, continuous monitoring and adjustment of fluid therapy.[16]

Eckerwall G et al. (2006) retrospectively studied 99 patients with severe acute pancreatitis, with 17% hospital mortality. Admission hypovolemia occurred in 13% (13/99) and was associated with increased mortality (P=0.009). During the first 3 days, patients received 11,000±4,100 mL fluids and 1,470±820 kcal, indicating potential areas for improving fluid and nutritional management.[17]

Du XJ et al. (2011) randomized 41 patients with severe acute pancreatitis to 6% Hydroxyethyl Starch (HES) 130/0.4 (n=20) or Ringer's Lactate (n=21). HES significantly reduced intra-abdominal pressure during days 2–7, decreased mechanical ventilation use (15.0% vs 47.6%), and achieved earlier negative fluid balance (2.5±2.2 vs 4.0±2.5 days), suggesting potential benefits in early severe AP resuscitation.[18]

Costea NC et al. (2025) randomized 108 patients with mild-to-moderate acute pancreatitis to dextran 40 plus Ringer's Lactate or Ringer's Lactate alone. Dextran significantly reduced CRP, while SIRS, organ failure, mortality, and complications were comparable. Hospital stay was 5 vs 6 days (P=0.1), with similar mild adverse events.[19]

Shu W et al. (2025) randomized 60 ICU patients with acute pancreatitis to 5% albumin plus crystalloids or crystalloids alone. Albumin did not improve SIRS remission or 60-day mortality, but reduced sepsis incidence (10% vs 36.7%, P=0.01).[20]

Futier E et al. (2020) conducted a multicenter randomized trial of 775 patients undergoing major abdominal surgery, comparing 6% HES 130/0.4 with 0.9% saline. Death or major complications at 14 days occurred in 36% vs 32% (RR 1.10, 95% CI 0.91–1.34; P=0.33), with no significant differences in secondary outcomes. Mortality at 28 days was 4.1% vs 2.3% (RR 1.76, 95% CI 0.79–3.94; P=0.17), providing no support for HES use.[21]

Zhao G et al. (2013) randomized 120 patients with severe acute pancreatitis to normal saline (NS), NS + HES, or NS + HES + glutamine. Compared with NS, the HES groups reached the endpoint earlier (3.9 ± 0.23 and 4.1 ± 0.21 vs. 5.8 ± 0.25 days; $P < 0.05$) and required less fluid (67.26 ± 28.53 and 61.79 ± 27.61 vs. 85.23 ± 21.27 mL/kg/day; $P < 0.05$). Renal dysfunction, Acute Respiratory Distress Syndrome (ARDS), Multiple Organ Dysfunction Syndrome (MODS), Abdominal Compartment Syndrome (ACS), infections, Intra-Abdominal Pressure (IAP), inflammatory markers, urinary Lactulose/Mannitol ratio (L/M ratio), and endotoxin levels were reduced, while mortality was not significantly different. The findings suggest that HES-based resuscitation, particularly with glutamine, may improve inflammation and intestinal barrier function in severe AP.[22]

Lipinski M et al. (2015) retrospectively studied 103 patients with acute pancreatitis treated with Ringer's lactate (RL) or normal saline (NS). No significant differences were found in pancreatic necrosis (25% vs. 19%; P = 0.637), enteral nutrition requirement (23 vs. 17; P = 0.534), mortality, or hospital stay (9 days in both groups; P = 0.776). RL did not improve clinical outcomes compared with NS.[23]

Wang ZF et al. (2004) reported that in 32 patients with severe acute pancreatitis, dexamethasone and dextran 40 improved abdominal pain within 4–8 hours; 27 recovered without surgery, while 5 required surgery and 4 died. The combination may reduce inflammation and improve microcirculation.[24]

Table: Studies Included and Key Findings on Fluid Resuscitation Strategies in Acute Pancreatitis

Author (Year)	Key findings
Wu BU et al., 2011	Lactated Ringer's significantly reduced SIRS and CRP levels compared with normal saline.
de-Madaria E et al., 2018	Lactated Ringer's solution may reduce systemic inflammation more effectively than normal saline in acute pancreatitis.
Choosakul S et al., 2018	LRS reduced early systemic inflammation but showed no significant advantage over NSS in later clinical outcomes.
Kayhan S et al., 2021	LRS significantly reduced moderate acute pancreatitis, CRP, and improved acid–base status compared with NSS.
Lee A et al., 2021	Compared LR with NS; primary outcome was changes in SIRS at 24 hours, with evaluation of disease severity, ICU admission, hospital stay, and adverse events.
Mao EQ et al., 2010	Rapid hemodilution increased sepsis and mortality, supporting a target hematocrit of 30%–40% during the acute phase.
Gardner TB et al., 2010	Early aggressive fluid resuscitation during the first 24 hours was associated with reduced mortality in severe acute pancreatitis.
Brown A et al., 2002	Persistent hemoconcentration at 24 hours was associated with the development of necrotizing pancreatitis, despite similar fluid resuscitation volumes.
de-Madaria E et al., 2011	>4.1 L fluid in 24 hr increased organ failure and complications, where as 3.1–4.1 L had favorable outcomes.
Warndorf MG et al., 2011	Early fluid resuscitation reduced SIRS and organ failure at 72 hours, with greatest benefit in interstitial pancreatitis.
Wall I et al., 2011	More aggressive fluid hydration may have contributed to reduced mortality by preventing pancreatic necrosis.

Kuwabara K et al. (2011)	Higher 48-hr fluid volume increased mortality in severe AP, while a higher FV48/FVH ratio was associated with lower mortality.
Eckerwall G et al., 2006	Admission hypovolemia was associated with increased mortality, highlighting the importance of adequate early fluid resuscitation.
Du XJ et al., 2011	Early HES-based fluid resuscitation may reduce intra-abdominal pressure and the need for mechanical ventilation.
Costea NC et al., 2025	Dextran 40 plus Ringer's Lactate improved early CRP response.
Shu W et al., 2025	Albumin supplementation did not significantly improve SIRS resolution or 60-day mortality, but reduced sepsis incidence.
Futier E et al., 2020	HES showed no clinical benefit over saline and provided no support for its use in fluid resuscitation.
Zhao G et al., 2013	Normal saline combined with HES and glutamine improved resuscitation in severe acute pancreatitis by reducing inflammation.
Lipinski M et al., 2015	Administration of Ringer's Lactate did not provide a significant clinical benefit over normal saline in acute pancreatitis.
Wang ZF et al., 2004	Dexamethasone and dextran 40 may attenuate severe acute pancreatitis by suppressing inflammatory mediators and improving microcirculation.

DISCUSSION & CONCLUSION

Wu BU et al. (2011) reported that Lactated Ringer's significantly reduced SIRS and CRP levels compared with normal saline.[5]

de-Madaria E et al. (2018) concluded that Lactated Ringer's solution may reduce systemic inflammation more effectively than normal saline in acute pancreatitis, although the overall evidence remains limited.[6]

Choosakul S et al. (2018) reported that LRS reduced early systemic inflammation but showed no significant advantage over NSS in later clinical outcomes.[7]

Kayhan S et al. (2021) found that LRS significantly reduced moderate acute pancreatitis, CRP, and improved acid–base status compared with NSS.[8]

Mao EQ et al. (2010) reported that rapid hemodilution increased sepsis and mortality, supporting a target hematocrit of 30%–40% during the acute phase.[10]

Gardner TB et al. (2010) reported that early aggressive fluid resuscitation during the first 24 hours was associated with reduced mortality in severe acute pancreatitis.[11]

Brown A et al. (2002) concluded that persistent hemoconcentration at 24 hours, indicating inadequate fluid resuscitation, was associated with the development of necrotizing pancreatitis, whereas adequate fluid resuscitation did not prevent pancreatic necrosis.[12]

de-Madaria E et al. (2011) reported that lower fluid administration during the first 24 hours was not associated with adverse outcomes, whereas higher fluid requirements were linked to poorer outcomes and required close monitoring.[13]

Warndorf MG et al. (2011) concluded that early fluid resuscitation reduced SIRS and organ failure at 72 hours, with the greatest benefit observed in patients with interstitial rather than severe pancreatitis.[14]

Wall I et al. (2011) suggested that more aggressive fluid hydration may have contributed to reduced mortality by preventing pancreatic necrosis in acute pancreatitis.[15]

Eckerwall G et al. (2006) reported that moderate fluid resuscitation, nutritional support, and less stringent glucose control in severe acute pancreatitis were associated with 17% mortality, highlighting opportunities to improve outcomes.[17]

Du XJ et al. (2011) concluded that early HES-based fluid resuscitation in severe acute pancreatitis may reduce intra-abdominal hypertension and the need for mechanical ventilation.[18]

Costea NC et al. (2025) reported that dextran 40 plus Ringer's Lactate improved early CRP response without increasing complications, although medium-term outcomes were comparable.[19]

Shu W et al. (2025) found that albumin supplementation did not significantly improve SIRS resolution or 60-day mortality in patients with acute pancreatitis.[20]

Futier E et al. (2020) found no significant difference in death or major postoperative complications with HES versus 0.9% saline at 14 days (36% vs 32%; RR 1.10, 95% CI 0.91–1.34; P=0.33). These findings do not support HES for volume replacement in high-risk surgical patients.[21]

Zhao G et al. (2013) concluded that normal saline combined with HES and glutamine improved resuscitation in severe acute pancreatitis by reducing inflammation and preserving intestinal barrier function.[22]

Lipinski M et al. (2015) concluded that early administration of Ringer's Lactate did not provide a significant clinical benefit over normal saline in acute pancreatitis.[23]

Wang ZF et al. (2004) concluded that dexamethasone and dextran 40 may attenuate severe acute pancreatitis by suppressing inflammatory mediators and improving microcirculation.[24]

Overall, the evidence suggests that early, individualized fluid resuscitation is important in acute pancreatitis. Lactated Ringer's solution generally reduced SIRS and CRP more effectively than normal saline, although clinical benefits were inconsistent. Excessive fluid administration and rapid hemodilution were associated with increased organ failure, sepsis, and mortality. HES-based and adjunctive therapies showed potential benefits in selected patients, but evidence regarding their safety and clinical effectiveness remains limited. Further large, well-designed randomized controlled trials are needed to establish optimal fluid type, volume, and

timing, and to determine the safety and clinical benefits of adjunctive therapies in acute pancreatitis.

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