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Fluid Therapy in Fluid Resuscitation of Patients with Traumatic Brain Injury: A Retrospective Cohort Study

Ramin Abrishami[1], Mehri Farhang Ranjbar[1], Mohammad Taqi Khan Mohammadi[1], Ali Dastjerdi[2], Mohammad Dastjerdi[1], Seyed Hadi Aghili[1*]

[1] Research Center for Trauma in Police Operations, Directorate of Health, Rescue & Treatment, Police Headquarter, Tehran, Iran.
[2] Research Committee of Sabzevar University of Medical Sciences, Sabzevar, Iran.

***Corresponding Authors**: Seyed Hadi Aghili, Research Center for Trauma in Police Operations, Directorate of Health, Rescue & Treatment, Police Headquarter, Tehran, Iran; Tel: 0098-1417944661; E-mail: seyedhadi.aghili2020@gmail.com.

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Abstract

Introduction: Traumatic brain injury (TBI) represents a critical medical condition imposing a substantial disease burden globally. Appropriate fluid resuscitation is essential for trauma recovery. This study evaluated optimal fluid strategies for TBI patients.

Methods: This cross-sectional study examined 358 traumatic brain injury patients admitted to the emergency department of a hospital in Mashhad from June 2018 to June 2021. Patients were categorized into four groups per total pre-hospital fluid volume received, five groups per fluid type received, and three groups per pre-hospital transport times. Variables, such as the Glasgow Coma Scale (GCS), blood pressure, mortality, and morbidity, were recorded.

Results: In patients with normal blood pressure, there was no difference in outcomes between normal saline versus balanced crystalloids. In hypotensive or severely injured patients with injury severity scores greater than 16, 1-2L normal saline was associated with shorter hospital stays than >2L fluids. Pre-hospital transport times < 15 minutes were correlated with lower mortality and shorter hospitalizations versus > 15 minutes.

Conclusion: Fluid volume impacts outcomes in traumatic brain injury. In hypotensive or severely injured patients (ISS>16), 1-2L normal saline was linked to shorter hospital stays versus >2L fluid volumes. The type of crystalloid did not affect outcomes in normotensive patients. Minimizing pre-hospital transport times below 15 minutes may improve patient survival and recovery. Optimizing fluid resuscitation protocols has the potential to improve traumatic brain injury prognosis.

Keywords: Trauma; Traumatic Brain Injury; Fluid Therapy; Fluid Resuscitation.

Introduction

Traumatic injuries remain a primary global health concern, accounting for a substantial proportion of the overall disease burden worldwide. Every year, about five million people die from trauma.[1-4] TBI caused by an external force acting upon the head can affect the brain's function. This type of trauma impacts the lives of millions of people every year. Among the most critical causes of TBI leading to hospitalization are falls (49.1%) and motor vehicle accidents (24.5%).[5] Generally, traumatic injuries are still the leading cause of mortality in people below 35 years, and 40% of deaths from trauma are caused by accidental hemorrhagic shock and its outcomes.[6,7]

Fluid resuscitation constitutes the initial intervention in the hemodynamic management of hemorrhagic and hypovolemic shock resulting from traumatic injury. The main aim of fluid therapy is to resolve blood circulation disorders after an accident.[8-11] Lost fluid resuscitation in patients with TBI is considered challenging because recommendations for the use and selection of available fluids are constantly being reviewed and discussed.[12,13] Besides trying to cease bleeding from external wounds and fractures, treatment of trauma patients is initiated by resuscitation with intravenous (IV) fluid (before or during rapid transport to a healthcare center). There is evidence indicating that IV fluid resuscitation before bleeding control may be accompanied by bleeding intensification (elevated blood pressure) and worsening of the patient's blood coagulation status (hemodilution).[14,15]

Moreover, excessive IV fluid resuscitation may lead to tissue edema.[15] Some studies have demonstrated that administering overly aggressive fluid resuscitation can lead to alterations in tissue perfusion and adverse effects like abdominal compartment syndrome and respiratory distress syndrome.[16,17] Therefore, prescribing more fluids is not always correct.[18] Recommendations change regarding the use of crystalloids, colloids, packed red blood cells, fresh whole blood, and clotting factors.[19] Other problems, such as resource availability, affect physicians' choice of fluid. Therefore, the best available fluid does not always match the proper fluid for the patient, especially when transferring a patient takes a long time and no blood is available.[20] Crystalloids encompass solutions ranging from hypertonic saline to Ringer's lactate. A key challenge is determining optimal first-line crystalloids for resuscitation. This is especially important for patients with central nervous system injuries, as the brain is susceptible to osmolality changes. Hypotonic fluids are not recommended for head injuries since they can worsen cerebral edema. Research is needed to identify the best crystalloid options for trauma patients at risk of brain edema.[21]

Evidence-based health policies can improve population health and equity in service delivery. Both global evidence and local data should inform policy decisions. Local evidence encompasses health system data on disease, risk factors, vital events, service coverage, and resources. This research on trauma fluid selection will provide local evidence to develop protocols that optimize patient outcomes, given limited resources.

Trauma is among the most common reasons patients visit hospitals' emergency departments. A variable spectrum from surface to severe injuries that lead to a patient's death makes systematic classification and correct triage of patients necessary. Early interventions are considered the main principle to reduce mortality rates and disabilities caused by trauma.[22] The way trauma patients are dealt with and the use of a pre-determined program to initially assess and recover patients can improve the patient's fate.[23] Therefore, this study evaluates the effect of fluid therapy type and volume received by the patient based on age, gender, trauma index, type of trauma, GCS, and blood pressure on morbidity and mortality within the first 24 hours of TBI patients' admission to the emergency department of a hospital in Mashhad during 2018-2021, and to use the findings to determine the roadmap for resuscitating patients in pre-hospital and hospital emergency conditions.

This study thus aims to choose the most appropriate form of fluid therapy and volume of fluid infused based on available resources in TBI patients so that the findings of this study can be used in health system policy-making.

Methods

Study Design and Ethics Approval

The present study was cross-sectional research conducted on TBI patients admitted to the emergency department of a hospital in Mashhad from June 2018 to June 2021. The administrative and legal procedures of the study were completed after receiving approval for the project and obtaining permission from the research ethics committee.

Data Collection

After examining the medical records of TBI patients, the complete demographic history was extracted. This included the GCS scores, trauma mechanism, existing underlying conditions, medication intake, alcohol consumption, and volume and type of infused fluid. Other variables were also extracted for analysis in this study. These included injury severity based on the Injury Severity Score (ISS) standard, pre-hospital infused fluids, systolic and diastolic blood pressures, attending physician's specialty type, mortality and morbidity indicators (need for hospital and intensive care unit (ICU) admission, need for mechanical ventilation) within the first 24 hours of admission, and number of days of hospital stay. An ISS of 1–8 is considered minor, 9–15 Moderate, 16 and higher severe, and very severe.[24] All data were recorded in a checklist designed based on the study objectives. Several faculty members approved the checklist.

Patient Outcomes

The condition of patients, completion of treatment course or death, and factors affecting this issue were investigated.

Inclusion Criteria

The study inclusion criteria were:

Patients aged more than 15 years,

No history of diabetes and renal diseases,

No alcohol and aspirin consumption,

Not suffering from diseases that lead to severe volume depletion and dehydration, such as gastroenteritis, Suffering from TBI.

Sample Size Calculation

Using the sample size estimation formula (n=(z_(1-α/2) ^2×p(1-p))/d^2) for prevalence studies, and considering the reliability level of 95%, the prevalence of hyperosmolarity in patients admitted to hospital that equals 0.30,[25] and acceptance of the error rate of 0.05, the sample size of the study was estimated to be 322. For further assurance, 358 TBI patients admitted to the emergency department of a hospital in Mashhad from March 21, 2018, to March 21, 2021, whose demographic data were complete and met the inclusion criteria, were included in the study. To select samples from the statistical population, the list of patients admitted to the hospital was prepared. Three hundred fifty-eight patients were then randomly selected using the random numbers table. As there were 217 defects in medical records regarding the prehospital data, these data were excluded from the study analyses.

Patient Grouping

Patients were categorized into four groups according to the total prehospital fluid volume received: 0-0.5L, 0.5-1L, 1-2L, and >2L. These groups were selected to reflect clinically meaningful volume cutoffs. Also, patients were classified based on the type of IV fluid received: normal saline, hypertonic, Ringer's solution, Ringer's lactate solution, and 1/3 solution. These represent the various crystalloid solutions used for prehospital resuscitation of trauma patients at the study hospital.

The fluid volume and type groups were compared for differences in hospital stay, mortality, morbidity, and physician specialty. The statistical significance of differences between type groups was determined using appropriate tests.

Statistical Analysis

The data was analyzed using SPSS 24.0 software. For qualitative variables, either the chi-square test or Fisher's exact test was utilized. For normally distributed quantitative variables, the analysis involved employing a one-way analysis of variance (ANOVA) followed by Tukey's post hoc test to assess pairwise differences between groups. For skewed quantitative variables, the Kruskal-Wallis test was utilized, followed by the Mann-Whitney post hoc test to evaluate differences between groups. A significance level of 5% (α=0.05) was considered for all statistical test.

Results

In this study, a total of 272 men and 86 women with an average age of 39.71±16.51 years were included.

The results presented in Table 1 delineate the condition of patients based on the volumes of fluid administered. It was observed that the mean systolic and diastolic blood pressure, as well as the Glasgow Coma Scale (GCS), were significantly lower in patients who received fluid intake exceeding 2 liters compared to those receiving less than 1 liter of fluid. Furthermore, the median Injury Severity Score (ISS) and the duration of hospitalization were notably higher in patients with fluid intake exceeding 2 liters than in those with fluid intake less than 1 liter ($p<0.001$). The highest mortality rate and the need for ventilator support were noted among patients with fluid volumes ranging from 1 to 2 liters, indicating variances in mortality and morbidity based on the volume of fluid administered($p<0.001$). Regarding prescription patterns, specialists in general surgery and emergency medicine predominantly prescribed fluid volumes ranging from 1 to 2 liters. In contrast, orthopedic specialists and neurosurgeons tended to prescribe more than 1/3 of the total fluid volume, specifically between 0.5 to 1 liter ($p<0.001$).

Table 1: Comparison of the mean GCS, blood pressure, injury severity, number of hospital stay days, morbidity and mortality, and the attending physician specialty in terms of the volume of fluid-infused.

The volume of infused fluid	0-0.5 liters (L)	0.5-1.0L	1.0-2.0L	>2.0L	Test result
GCS	14.80±0.64	14.52±0.94	13.82±1.61	13.45±2.01	F=16.31,p<0.001
Systolic blood pressure within 24 hours after the accident	117.96±11.63	114.78±11.56	107.60±15.84	97.25±19.54	F=24.95,p<0.001
Diastolic blood pressure within 24 hours after the accident	72.34±10.84	68.95±9.86	65.35±12.33	57.37±12.60	F=18.18,p<0.001
Injury severity	5(5-8)	8(8-13)	17(10-26)	29(18-39.25)	χ2=134.61,p=0/001
Number of hospital stay days	5(4-5)*	5(4-6)	7(6-8)	9(7.5-11)	χ2=109.40, p<0.001
Mortality					
Discharge	81 (23/1)	139 (39/7)	93 (26/6)	37 (10/6)	χ2=12.49 p=0.001
Death	0 (0)	0 (0)	5 (62/5)	3 (37/5)	
Morbidity					
Admission to the ward	79(27.8)	128(45.1)	66(23.2)	11(3.9)	χ2=88.11 p<0.001
Admission to ICU	2(3.3)	9(15)	24(40)	25(41.7)	
Need for ventilator	0(0)	2(25)	4(50)	2(25)	
Specialty					
Emergency medicine	0(0)	0(0)	4(80)	1(20)	χ2=79.21 p<0.001
Generic surgery	9(11)	21(25.6)	28(34.1)	24(29.3)	
Neurosurgeon	6(8.7)	28(40.6)	25(36.2)	10(14.5)	
Orthopedist	66(32.7)	90(44.5)	41(20.3)	5(2.5)	

Values are shown as mean±SD for and number (%) for continuous and categorical variables, and for skewness variable median (IQR)
For normal quantitative variables one-way analysis of variance test, for skewness variables Kruskal-Wallis test, for qualitative variables, chi-square or Fisher tests.

In Table 2, the patient's conditions were categorized based on the types of fluids administered. The mean systolic and diastolic blood pressure and the Glasgow Coma Scale (GCS) were reported to be significantly lower in patients receiving Ringer's solution fluid compared to those receiving normal saline and 1/3 saline(p<0.001). In this study Injury severity score is divided into three groups, including mild (168 patients, %46/93), moderate (77 patients, %21/51), severe, and very severe (113 patients, %31/56). The median Injury Severity Score (ISS) in patients receiving Ringer's solution fluid was notably higher than in those receiving 1/3 saline and Ringer's lactate solution (p<0.001). The highest mortality rate, along with the need for ICU admission and ventilator support, was observed among patients receiving normal saline, indicating variations in mortality and morbidity based on the type of fluid administered (p<0.001). Specialists in general surgery, neurosurgery, and emergency medicine predominantly prescribed normal saline, whereas orthopedic specialists prescribed 1/3 saline more frequently than normal saline (p<0.001).

According to the findings presented in Table 3, patients with Injury Severity Score (ISS) exceeding 16 are categorized as severe or very severe cases. The results from the table above indicated that among patients with

ISS greater than 16, those who received normal saline at a volume ranging from 1 to 2 liters exhibited a shorter duration of hospitalization compared to those who received a fluid therapy volume exceeding 2 liters (p=0.004). Additionally, among individuals with a systolic blood pressure below 90 mm Hg, those who received normal saline at 1-2 liters had a shorter hospitalization period than those with a fluid therapy volume exceeding 2 liters (p=0.003).

In Table 4, we investigated the association between the length of hospital stay and morbidity concerning the time taken to reach the hospital. It was observed that individuals who reached the hospital in less than 15 minutes had a significantly shorter average length of hospital stay compared to those with transportation times exceeding 15 and 30 minutes. Additionally, a noteworthy correlation was found between morbidity and the time taken to reach the hospital, with 50% of patients requiring ventilators and 53.33% of patients needing ICU admission reaching the hospital within 15 to 30 minutes.

Table 2: Comparison of the mean GCS, blood pressure, injury severity, number of hospital stay days, morbidity and mortality, and the attending physician specialty in terms of the type of fluid-infused.

Type of infused fluid	Normal saline	Hypertonic	Ringer's solution	Ringer's lactate solution	1/3 solution	Test result
GCS	14.3±1.47	12.0±0.0	10.50±3.87	15.0±0.0	14.74±0.57	F=17.13,p<0.001
Systolic blood pressure within 24 hours after the accident	105.96±14.39	100.0±0.0	81.25±21.74	125.0±0.0	120.79±9.88	F=34.45,p<0.001
Diastolic blood pressure within 24 hours after the accident	63.16±10.62	60.0±0.0	52.50±14.43	85.0±0.0	74.09±10.15	F=26.03,p<0.001
Injury severity	13(8-25)	25(25-25)	28.50(9.25-53.75)	5(5-5)	8(5-13)	χ2=28.59,p<0.001
Number of hospital stay days	6(5-8)	9(9-9)	5(5-5)	2(2-2)	5(4-6)	χ2=4.60,p=0.20
Mortality						
Discharge	202(57.9)	1(0.3)	1(0.3)	1(0.3)	144(41.3)	χ2=28.37 p<0.001
Death	5(62.5)	0(0)	3(37.5)	0(0)	0(0)	
Morbidity						
Admission to the ward	146(51.4)	1(0.4)	1(0.4)	1(0.4)	135(47.5)	χ2=40.76 p<0.001
Admission to ICU	50(84.7)	0(0)	0(0)	0(0)	9(15.3)	
Need for ventilator	7(87.5)	0(0)	1(12.5)	0(0)	0(0)	
Specialty						
Emergency medicine	3(60)	0(0)	2(40)	0(0)	0(0)	χ2=140.96 p<0.001
Generic surgery	69(85.2)	0(0)	2(2.5)	0(0)	10(12.3)	
Neurosurgeon	54(78.3)	1(1.4)	0(0)	0(0)	14(20.3)	
Orthopedist	81(40.1)	0(0)	0(0)	1(0.5)	120(59.4)	

Values are shown as mean±SD for and number (%) for continuous and categorical variables, and for skewness variable median (IQR); For normal quantitative variables one-way analysis of variance test, for skewness variables Kruskal-Wallis test, for qualitative variables, chi-square or Fisher tests.

Table 3: Comparison of the number of hospital stay days in terms of the type of fluid-infused in severe trauma.

	ISS>= 16		Result test	SBP<90		Test result
The volume of infused fluid	1.0-2.0 L	>2.0 L		1.0-2.0 L	>2.0 L	
Number of hospital stay days	8.8±2.44	10.4±2.81	P=0.004	8.76±3.46	11.23±2.20	P=0.003
Values are shown as mean±SD; For normal quantitative variables one-way analysis of variance test						

Table 4: Comparison of the number of hospital stay days, in terms of the Prehospital Transport Time.

Prehospital Transport Times	< 15 minutes	15-30 minutes	>30 minutes	Test result
Number of hospital stay days	5(4-6)	6(4-8)	6(4-9)	χ2=12.8, p=0.002
Morbidity				
Admission to the ward	146 (51.41)	110 (38.73)	28 (9.86)	χ2=23.489 p<0.001
Admission to ICU	13 (21.66)	32 (53.33)	15 (25)	
Need for ventilator	2(25)	4(50)	2(25)	
Values are shown as numbers (%) for continuous and categorical variables and skewness variable median (IQR) For normal quantitative variables one-way analysis of variance test, for skewness variables Kruskal-Wallis test, for qualitative variables, chi-square or Fisher tests.				

Discussion

TBI represents a significant contributor to mortality and long-term physical impairment. Annually, an estimated 12 million people worldwide are affected by TBI. This injury is considered a significant health and socioeconomic problem across the world, imposing substantial costs on healthcare systems.[26] Providing maintenance fluids is considered standard care for critically ill TBI patients. The amount and type of maintenance fluids administered can influence the pathophysiology of secondary brain injury in these patients.[27,28] The proper approach to fluid administration is to maintain cerebral arterial pressure and deliver oxygen to the brain. Regarding red blood cell (RBC) transfusion, the classical approach was to transfuse RBCs in TBI patients to maintain hemoglobin levels >10 g/dL or hematocrit >30% to sustain oxygen-carrying capacity. However, clinical practice has recently moved towards a more restrictive approach (hemoglobin ≥7 g/dL) because research studies have shown that the previous approaches (hemoglobin ≥10 g/dL) may be ineffective or even harmful in critical care settings.[27] Increasing IV fluid to increase blood pressure, tissue perfusion, and oxygen delivery can improve and treat this condition. A method that yields similar or better resuscitation results with lower fluid volumes would be very beneficial.[29]

Blood pressure management is essential in acute brain injury to prevent secondary injury.[30] A 2014 meta-analysis found solutions with >0.9% salt increased blood pressure in TBI patients compared to normal saline.[31] However, there is no evidence that any fluid type improves short- or long-term TBI outcomes.[32] A study by Muller showed higher systolic pressure with Ringer's lactate versus other fluids in animals.[33] The difference is that Muller's study used animals. One study showed that TBI fluid intake should achieve optimal volume for each patient. Hypertonic fluids may improve diastolic pressure in TBI. Muller's study found that Ringer's lactate did not restore diastolic pressure in animals.[33]

The mean hospital stay with 0.5-1 L fluid was significantly shorter than with 1-2 L (p<0.001) and >2 L (p<0.001). There was no significant difference in hospital stay based on fluid type. Some studies have shown that fluid volume can impact hospital stay in TBI patients, while others found no effect of fluid volume on stay. More research is needed to draw definitive conclusions on the effects of fluid administration on TBI patient outcomes. One study found electrolyte solutions reduced hospital stay and mortality compared to colloids in TBI.[34] Another study showed that fluid intake >2L in TBI patients led to higher GCS and lower mortality.[35] However, one study found no effect of fluid volume on TBI patients' hospital stay.[36]

TBI causes the most mortality and long-term disability globally, affecting ~70 million people annually.[37] In this study, among patients who died, 5 received 1-2 L fluid. Mortality frequency differed significantly based on fluid volume ($p=0.001$) and type ($p<0.001$); 5 of 8 deaths received normal saline. A study by Dash et al.[38] in 2125 ICU TBI patients found positive (0.85-1.13 L) and high (1.48-4.32 L) fluid balances associated with increased mortality.[39] These results agree with the present study. A 2018 review found no advantage of colloids over crystalloids, and the SAFE trial showed higher mortality with albumin than saline. TBI is often accompanied by acute kidney injury (9-23%) and higher mortality. Colloids increase the risk of acute kidney injury and replacement therapy in critically ill patients. Recent Cochrane reviews found no superiority of colloids over crystalloids for mortality. A study by Cheng et al. (2018) found no significant mortality difference between mannitol and HTS. Comparable 6-month mortality and in-hospital deaths were reported between groups.[40] The available evidence suggests that mannitol and HTS have no clear superiority over one another. However, further research is still needed.[37] Moreover, hyperosmolar therapy with HTS can significantly reduce intracranial pressure (ICP), which may prevent secondary injury in TBI patients. Based on current evidence, the effectiveness of HTS is similar to mannitol, the gold standard treatment for lowering ICP and mortality in TBI.[37] However, another study found no effect of fluid volume on TBI mortality.[41] Among ventilated patients, 4 received 1-2 L fluid. Ventilation needs differed significantly by fluid volume ($p<0.001$) and type ($p<0.001$); 7 received normal saline. A 2016 review found that randomized trials show that IV fluid type, dosage, and schedule can impact outcomes in surgical and critically ill patients, but optimal approaches remain debated.[42] An observational study of 30,994 surgery patients found 9.9% saline increased risks of infection, kidney injury, replacement therapy, and complications versus crystalloids.[43] Susanto et al. (2022) investigated the optimum dose and concentration of hypertonic saline in traumatic brain injury in a review study. Eleven research found that hypertonic saline and mannitol were equally effective, whereas eight studies reported that hypertonic saline performed better. According to this study, 3% hypertonic saline at a therapeutic dose of 1.4 to 2.5 mL/kg as a bolus is a perfect concentration.[44]

In the study by Paravar et al. (2014), which was conducted on 2000 pre-hospital patients, in-hospital trauma mortality was higher in patients with severe injuries and prolonged pre-hospital transport times. When the pre-hospital transport time to definitive care was shorter (less than 10-15 minutes), and patients were well selected, delayed resuscitation appeared to be an excellent option to reduce morbidity and mortality.[45] The findings of that study are consistent with the present study. Furthermore, the study by Nasser et al. (2020), which was conducted on about 43 thousand patients, demonstrated that every minute increase in pre-hospital response time was independently associated with a 2% rise in mortality. The results of that study verified the scoop-and-run approach.[46] Additional studies have exhibited that when the pre-hospital transport time exceeded 10-15 minutes, mortality escalated, and targeted resuscitation with low-volume crystalloids and basic/advanced supportive interventions conferred an enhanced prognosis for the patients.[47,48]

This study has several limitations. First, it was conducted at a single hospital, so the results may not be generalizable to other settings. Second, as a retrospective study based on medical records, data accuracy and completeness depend on record quality. Important clinical details may be missing. Third, we lacked data on long-term outcomes, so we could not evaluate the impact of fluid therapy beyond the initial hospitalization. Finally, protocols for fluid administration and other aspects of care may have changed over the study period. A prospective study randomized to different fluid protocols with longer-term follow-up could provide higher-quality evidence. However, this initial study provides valid real-world data to guide clinical practice and future research to optimize fluid resuscitation in TBI patients.

Conclusion

In conclusion, the type and amount of prescribed fluid therapy affect the recovery of concussion patients and the function of their organs. Prescribing excessive fluid requirements may lead to organ dysfunction. In hypotensive or severe trauma patients, the administration of 1-2 liters of normal saline serum has a better prognosis than a larger volume. In normotensive patients, there is no significant difference between normal saline and 1/3 saline.

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Conflict of Interest Disclosures

The authors declare that they have no conflict of interest.

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Authors' Contributions

All the authors contributed to designing, collecting, analyzing, and editing the final manuscript.

Ethical Statement

This study was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences, with the ethics code IR.SBMU.TEB.POLICE.REC.1402.017.

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