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Original Article

Efficacy comparison of restrictive versus massive fluid resuscitation in patients with traumatic hemorrhagic shock

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Abstract: Objective: To compare the therapeutic effect and safety of restrictive versus massive fluid resuscitation in patients with traumatic hemorrhagic shock (TSH). Methods: Ninety TSH patients treated in the ICU of the Second Affiliated Hospital of Zhejiang University School of Medicine from June 2020 to January 2021 were recruited for this retrospective study. Among them, 47 cases received restrictive fluid resuscitation (RFR) after admission who were considered as the observation group (OG), while the other 43 cases were given massive fluid resuscitation (MFR) who were treated as the control group (CG). The clinical indices, coagulation function, blood gas analysis, mortality within 72 h, duration of mechanical ventilation, and ICU stay were compared between the two groups, and the amount of resuscitation fluid given and complications that occurred during treatment were recorded. Multivariate logistic regression analysis was used to screen the independent risk factors for complications. Results: In comparison to the CG, the resuscitation time, infusion volume, and lactate level in the OG were lower after treatment, while the hemoglobin level and blood gas residual base value (BE) were higher. Besides, the activated partial thromboplastin time (APTT), thrombin time (TT) and prothrombin time (PT) levels and arterial blood carbon dioxide partial pressure ($PaCO_2$) in the OG were lower, while arterial blood oxygen partial pressure (PaO_2) and pH were higher. The duration of mechanical ventilation and ICU stay in the OG after treatment were lower, and there was no statistical difference in mortality and complication rates within 72 h. Lower mean arterial pressure (MAP), higher APACHE II (Acute Physiology and Chronic Health Evaluation II) and longer resuscitation time were independent risk factors for complications in patients with traumatic shock. Conclusion: TSH treatment with RFR can effectively accelerate patients' resuscitation with less volume of infusion of resuscitation fluid, reduced time of mechanical ventilation and ICU hospitalization, and promote the recovery of coagulation function. It has good effects and is very suitable for clinical application.

Keywords: Restrictive fluid resuscitation, massive fluid resuscitation, traumatic hemorrhagic shock, coagulation function

Introduction

As traffic, industry, construction and transportation industries develop rapidly, there are more and more traumatic injuries caused by traffic accidents, industrial injuries, falling injuries and natural disasters [1, 2]. According to the World Health Organization, 5.8 million people die from trauma every year, and severe trauma has gradually become one of the leading causes of death among young people worldwide, of which 1/3 are attributed to bleeding. Hemorrhagic shock is one of the most common causes of death in trauma patients, accounting for 30% and 40% of deaths within 24 h after trauma [3, 4]. Traumatic hemorrhagic shock (THS) is characterized by severe injuries, rapid changes, high rate of missed diagnoses and high mortality, and is therefore often seen by emergency departments as well as surgeons [5, 6]. THS patients are prone to hypothermia, acidosis and coagulation dysfunction, which can gradually form in organs when the body is in a hypercoagulable state [7]. Coagulation factors are continuously consumed and circulating blood volume decreases dramatically, and patients may die of organ failure during ischemia and hypoxia, so adequate fluid resuscitation is needed to reduce these injuries [8, 9].

Fluid resuscitation is a rescue treatment with rapid intravenous infusion that is used until blood pressure is normalized, which improves the survival of THS patients to some extent [10]. It has also been mentioned that the administration of large amounts of fluids may not exert an effect in some patients but may even accelerate the progression of the disease [11]. In contrast, some researchers have proposed a more conservative method of infusion, which limits the rate of infusion to maintain patients' blood pressure at a low level, that is, restrictive fluid resuscitation (RFR) [12]. Owattanapanich et al. [13] mentioned that RFR could reduce mortality rates and seems to be associated with fewer complications such as coagulopathy, cardiovascular failure, respiratory failure and acute kidney injury. However, the conclusions on the way of applying RFR to THS patients and its effects are not yet uniform across countries.

Therefore, the effects of RFR and MFR were assessed and compared through the clinical data of THS patients.

Data and methods

Patient data

Ninety TSH patients admitted to the ICU of the Second Affiliated Hospital of Zhejiang University School of Medicine from June 2020 to January 2021 were enrolled in this retrospective analysis. Among them, 47 received RFR after admission and were regarded as the observation group (OG), with a mean age of (46.51±4.86) years, including 28 males and 19 females. The rest of the 43 patients received MFR and were set as the control group (CG), with a mean age of (47.54±5.07) years, including 23 males and 20 females. The injury severity score (ISS) was assessed immediately after the patient was evaluated for injuries in the six anatomical regions: head and neck, face, body surface, extremities, chest, abdomen, and pelvis (judged on the basis of radiographs, CT, and surgical findings). Injuries were scored from 1 to 5 points in order from mild to severe, and the 3 regions with the most severe injuries were selected for scoring. The degree of injury was assessed by the sum of the squares of the 3 scores, with a total score of 1 to 75 points, <17 points for mild injuries and ≥17 points for severe injuries.

The research was approved by the Medical Ethics Committee of the Second Affiliated Hospital of Zhejiang University School of Medicine, and all patients provided informed consent forms in accordance with the Declaration of Helsinki (20220485).

Inclusion and exclusion criteria

Inclusion criteria: Patients admitted to the hospital due to trauma, and thoes who met the diagnostic criteria of shock [14]; Patients with an age ≥18 years old; Patients with a time period less than 6 h from injury to admission; Patients with a shock index greater than 1 (Shock index = pulse rate/systolic blood pressure; Shock index ≤0.5 indicates no shock; An index = 1 suggests a loss of 20%-30% of blood volume; An index >1 indicates a loss of 31%-50% of blood volume, suggesting shock); Patients with complete clinical information.

Exclusion criteria: Patients with coagulation disorders; Patients with shock due to other reasons; Patients with substantial organ dysfunction; Patients with mental abnormalities or psychiatric-related illnesses; Patients who died before resuscitation after admission to hospital; Pregnant or breastfeeding women.

Treatment options

After admission, all patients were quickly assessed, their airways were maintained and vital signs were monitored, intravenous access was established, and hemostasis was applied to the injured area. Active hemostatic treatment was given along with rehydration therapy. The resuscitation solution used in both groups was colloid and crystalloid in a 1:3 ratio. Colloid: albumin (lot number: 201501A063, Swiss jetbelin Biological Products Co., Ltd). Crystalloid: normal saline (lot number: 1501251, Otsuka Pharmaceutical Co., Ltd., Guangdong, China), sodium potassium magnesium calcium glucose injection (lot number: 1652536，Jiangsu Hengrui Pharmaceutical Co., Ltd).

In the CG, a large amount of fluid resuscitation was implemented. Crystalloids and colloids were given via intravenous access in a ratio of approximately 3:1. With active fluid resuscitation and rapid correction of blood perfusion, the infusion rate was controlled at 10-15 mL/(kg·h) to keep the MAP in the range of 60-80 mmHg, and the total normal dose for both groups was >2600 mL. In the OG, the amount of resuscitated fluids was restricted, again with a ratio of crystalloids to colloids of approximately 2-3:1. When the mean arterial pressure was lower than 50 mmHg, the infusion rate was controlled at 20 mL/(kg·h). After reaching 50 mmHg, the infusion rate was gradually reduced and adjusted to make the mean arterial pressure at 50-60 mmHg.

Outcome measures

(1) Altogether 5 mL of peripheral venous blood was drawn from patients of both groups before and after treatment, and serum lactate was tested by blood lactate tester. The hemoglobin level was assessed by Japanese SysmexXN-1000 automatic hematology analyzer. The activated partial thromboplastin time (APTT), thrombin time (TT), and prothrombin time (PT) were measured using the Japanese Sysmex CA7000 automatic coagulation analyzer, and the blood lactate, arterial blood carbon dioxide partial pressure ($PaCO_2$), arterial blood oxygen partial pressure (PaO_2), pH, and blood gas residual base value (BE) were measured using the American GEM Premier 3000 blood gas analyzer. (2) The resuscitation time and total infusion volume of patients in both groups were counted. (3) The incidence of complications was compared between groups, including disseminated intravascular coagulation (DIC), acute respiratory distress syndrome (ADRS), and multiple organ dysfunction syndrome (MODS). (4) The duration of mechanical ventilation, ICU stay and death within 72 h in both groups were counted.

Statistical approach

Data were statistically analyzed using SPSS 20.0 software (SPSS Ltd., Chicago, USA). Continuous variables were expressed as number of cases, mean value, and standard deviation. Independent t-test was applied to assess data between the two groups and paired t-test was used for comparing different time periods in the same group and the results were expressed using t. For categorical variables, data were represented as the number of cases or percentages and tested using chi-square analysis, with the results shown as X^2. Multivariate logistic regression analysis was used to detect the independent risk factors of complications. P<0.05 was considered statistically significant.

Results

Baseline data

There was no statistical difference between groups in terms of age, gender, cause of injury, site of injury, shock index, ISS score, time from injury to resuscitation, heart rate (HR), and MAP (all P>0.05) (**Table 1**).

Comparison of clinical indices between groups

The clinical indices of both groups were counted, and the resuscitation time and infusion volume of the OG were lower than those of the CG (all P<0.05). There was no obvious difference in lactic acid, hemoglobin and BE before treatment (all P>0.05). However, the lactate level in the OG after treatment was lower, while the hemoglobin was higher, with statistical differences (all P<0.05) (**Table 2**).

Changes in coagulation function of patients before and after treatment

The coagulation function indices APTT, TT and PT of both groups were measured before and after treatment. The three revealed no obvious difference before treatment (P>0.05), while the levels increased after treatment (P<0.05). The levels in the OG were significantly lower than those in the CG (P<0.05) (**Figure 1**).

Blood gas analysis of two groups of patients before and after treatment

Comparing the $PaCO_2$, PaO_2, and pH values of blood gas analysis indexes before and after treatment, we found that there was no statistical difference before treatment (P>0.05). After treatment, the $PaCO_2$ decreased, while the PaO_2 and pH increased. The $PaCO_2$ of the OG was lower than that of the CG, while the PaO_2 and pH value of the OG were dramatically higher (P<0.05) (**Figure 2**).

Comparison of mechanical ventilation and clinical outcomes

After treatment, the mechanical ventilation and ICU hospitalization time in the OG were lower than those in the CG (P<0.05). The mortality within 72 h in the OG was 2.13%, slightly lower

Table 1. Baseline data

	Observation group (n=47)	Control group (n=43)	t/X^2	P
Age (year)	46.51±4.86	47.54±5.07	0.984	0.328
Gender			0.338	0.561
Male	28 (59.57)	23 (53.49)		
Female	19 (40.43)	20 (46.51)		
Cause of injury			0.489	0.783
Falling injury	6 (12.77)	4 (9.30)		
Traffic injury	38 (80.85)	35 (81.40)		
Crush injury	3 (6.38)	4 (9.30)		
Injured area			1.148	0.766
Brain injury	14 (29.79)	13 (30.23)		
Chest trauma	13 (27.66)	8 (18.60)		
Closed abdominal injury	11 (23.40)	12 (27.91)		
Limb and pelvic injuries	9 (19.15)	10 (23.26)		
Shock index	1.99±0.31	2.02±0.25	0.502	0.616
ISS scores	21.45±2.60	21.84±1.88	0.809	0.421
Time from injury to rescue (min)	101.89±21.91	99.4±18.38	0.581	0.563
Heart rate (time/min)	134.04±12.54	134.84±10.27	0.329	0.742
MAP (mmHg)	53.17±5.86	51.44±5.5	1.441	0.153
APACHE II	20.55±2.75	19.93±2.95	1.032	0.31

Note: ISS score: Injury Severity Score; MAP: Mean Arterial Pressure; APACHE II: Acute Physiology and Chronic Health Score.

Table 2. Clinical indicators

	Recovery time (min)	Infusion volume (mL)	Lactate (mmol/l)		Hemoglobin (g/l)		BE (mmol/L)	
			Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group (n=47)	77.85±6.92	1975.02±148.39	10.29±0.62	5.14±0.58	64.84±9.11	97.54±10.30	-7.30±2.12	-4.51±1.4
Control group (n=43)	98.05±10.71	3118.35±233.31	10.08±0.63	5.89±0.72	65.35±8.64	80.04±9.83	-7.23±1.84	-5.58±1.67
t	10.720	27.980	1.593	5.463	0.272	8.228	0.868	3.304
P	<0.001	<0.001	0.115	<0.001	0.786	<0.001	0.167	0.001

Note: Blood Gas Residual Base Value (BE).

than 4.65% in the CG, but the difference was not statistically different (P>0.05) (**Table 3**).

Comparison of incidence of complications between groups

The incidence of DIS, ARDS, MODS, and total complications between groups revealed no statistical difference (all P>0.05) (**Table 4**).

Univariate analysis of risk factors for complications

We compared the clinical data of 10 patients with complications and 80 patients without complications, and found that there were differences in shock index, ISS score, time from injury to rescue, heart rate, MAP, APACHE II and resuscitation time between the two groups(all P<0.05) (**Table 5**).

Multivariate analysis of risk factors for complications

The multivariate logistic regression analysis of the indicators with differences in the univariate analysis revealed that lower MAP, higher APACHE II and longer resuscitation time were independent risk factors for complications in patients with traumatic shock, as shown in **Table 6**.

Discussion

TSH patients have been resuscitated with more active fluid resuscitation, including early, mas-

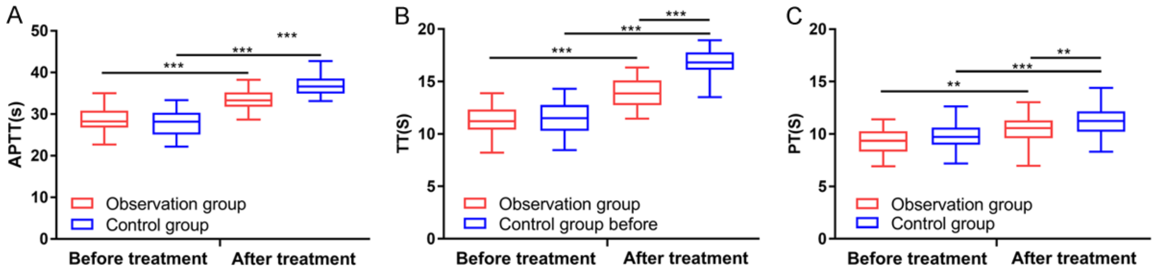

Figure 1. Changes of blood coagulation function of patients before and after treatment. A. APTT was elevated in both groups after treatment and as lower in the OG; B. TT was elevated in both groups after treatment and was lower in the OG; C. PT was elevated in both groups after treatment and was lower in the OG. Note: OG: Observation Group; CG: Control Group; ** indicates P<0.01; *** indicates P<0.001.

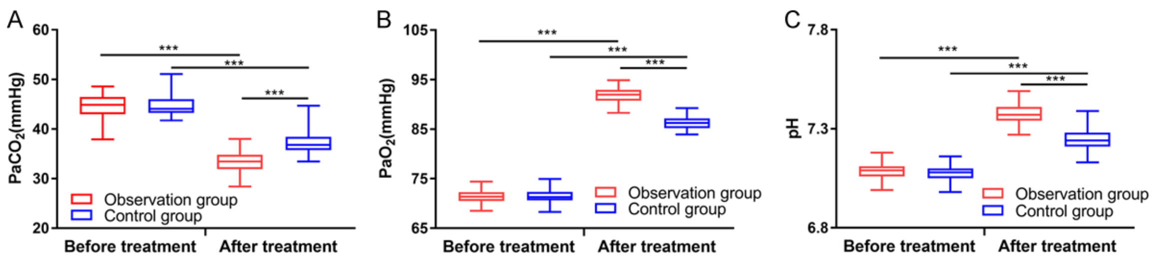

Figure 2. Blood gas analysis before and after treatment in both groups. A. $PaCO_2$ was decreased in both groups after resuscitation treatment and was lower in the OG; B. PaO_2 was elevated in both groups after resuscitation treatment and was higher in the OG; C. pH was elevated in both groups after resuscitation treatment and was higher in the OG. Note: OG: Observation Group; CG: Control Group; *** indicates P<0.001.

Table 3. Comparison of mechanical ventilation and clinical outcomes

	Mechanical ventilation time (h)	ICU stay (day)	Death within 72 h
Observation group (n=47)	7.7±1.34	8.83±2.09	1 (2.13)
Control group (n=43)	10.1±1.89	11.86±2.49	2 (4.65)
t	6.995	6.271	0.444
P	<0.001	<0.001	0.505

Table 4. Incidence of complications

	Observation group (n=47)	Control group (n=43)	X^2	P
Disseminated intravascular coagulation	1 (2.13)	1 (2.33)	0.001	0.949
Acute respiratory distress syndrome	2 (4.26)	3 (6.98)	0.317	0.573
Multiple organ dysfunction syndrome	1 (2.13)	2 (4.65)	0.444	0.505
Total complications	4 (8.51)	6 (13.95)	0.674	0.412

sive, and rapid replenishment of colloid or crystalloid fluids, which increases their mean systolic and arterial pressure levels and improves the perfusion of vital organs [15, 16]. However, excessive rehydration can lead to excessive dilution of the blood and may exacerbate coagulation dysfunction of patients in shock [17]. Krzych et al. [18] confirmed that MFR may have an impact on the function of platelets and coagulation factors by diluting them, thus leading to coagulation disorders. Thus, researchers believe that while ensuring blood perfusion of vital organs in patients who are in shock, it is not necessary to replenish fluid too actively and excessively. On the basis of stable maintenance of mean arterial pressure or systolic blood pressure, RFR relieves the related internal environment disorder.

Table 5. Univariate analysis table

	Complications (n=10)	No complications (n=80)	t/X^2	P
Age (year)	45.50±4.77	47.19±4.98	1.016	0.312
Gender			0.814	0.367
Male	7 (70.00)	44 (55.00)		
Female	3 (30.00)	36 (45.00)		
Cause of injury			3.579	0.167
Falling injury	2 (20.00)	8 (10.00)		
Traffic injury	6 (60.00)	67 (83.75)		
Crush injury	2 (20.00)	5 (6.25)		
Injured area			0.147	0.986
Brain injury	3 (30.00)	24 (30.00)		
Chest trauma	2 (20.00)	19 (23.75)		
Closed abdominal injury	3 (30.00)	20 (25.00)		
Limb and pelvic injuries	2 (20.00)	17 (21.25)		
Shock index	2.18±0.26	1.98±0.28	2.145	0.035
ISS scores	23.00±3.13	21.46±2.12	2.046	0.044
Time from injury to rescue (min)	113.90±16.22	99.05±20.15	2.238	0.028
Heart rate (time/min)	132.40±11.09	134.68±11.54	0.591	0.556
MAP (mmHg)	47.40±4.35	52.96±5.59	3.027	0.003
APACHE II	22.30±2.11	20.00±2.83	2.480	0.015
Recovery time (min)	96.10±9.65	86.43±13.55	2.183	0.032
Infusion volume (mL)	2565.00±601.93	2515.81±609.74	0.241	0.810

Note: ISS Score: Injury Severity Score; MAP: Mean Arterial Pressure; APACHE II: Acute Physiology and Chronic Health Score.

Table 6. Multivariate analysis table

	B	S.E.	Wals	Sig.	Exp (B)	95% C.I. of EXP (B)	
						lower limit	upper limit
MAP	-0.291	0.126	5.299	0.021	0.748	0.584	0.958
APACHE II	0.382	0.187	4.147	0.042	1.465	1.014	2.115
Infusion volume (mL)	0.104	0.050	4.275	0.039	1.110	1.005	1.225

Note: MAP: Mean Arterial Pressure; APACHE II: Acute Physiology and Chronic Health Score.

First of all, the recovery time of patients treated with RFR was faster than that of those with MFR, and the level of lactic acid after RFR is also lower. Because the restoration of tissue and organ blood perfusion in the application of RFR can reduce the adverse effects of infusion on the body, it maintains the balance of oxygen consumption and delivery, and helps the body repair faster [19]. The main cause of death in THS patients is severe coagulation disorder [20]. While analyzing the coagulation function of patients with different resuscitation methods, we found that the APTT, TT and PT levels were elevated in both groups after treatment, and the levels were lower after RFR than after the MFR, indicating that RFR was more effective in improving coagulation disorders. Traumatic blood loss leads to the loss of clotting factors, coupled with compensatory transfer of body fluids, and subsequent active rehydration all result in the dilution of those factors [21]. In this research, blood gas analysis revealed that both groups had metabolic acidosis and carbon dioxide retention before rescue. After resuscitation by both resuscitation methods, acidosis improved more obviously in the RFR group, and those patients had higher partial pressure of oxygen and lower partial pressure of carbon dioxide after treatment, suggesting the importance of RFR on blood gas analysis. ARDS that develops from THS is mainly associated with transfusion-related acute lung injury, while lung injury is caused by ischemia-reperfusion injury after hemorrhagic shock [22, 23]. Both groups developed ARDS during resuscitation and had a lower incidence of RFR, but did not manifest statistical differences because neither group had a high overall incidence. There was also no statistical difference in terms of 72-hour mortality, but the duration of mechanical ventilation and ICU were lower after RFR treatment, which also suggested that RFR was more beneficial to patients' recovery. Zhou et al. [24] compared the role of RFR and MFR in patients with septic shock and found that the former could better improve patients' cardiac function and clinical symptoms, which is similar to our study. RSR also reduced the mortality and complication rate of patients. After that, we found through multivariate analysis that lower map, higher APACHE II and longer resuscitation time were independent risk factors for complications of patients. Therefore, we should pay attention to these factors in the treatment process to bring better curative effect for patients.

This study not only explored the effects of the two resuscitation modalities on coagulation and blood gas indices, but also compared data on patients' mechanical ventilation and clinical outcomes. Although this research has some guiding significance for fluid resuscitation in THS patients, there are some shortcomings. Since this research lacks an assessment of patients' long-term survival and quality of life, as well as a detailed analysis of the causes of adverse reactions in the course of treatment, these are areas we can research further in the future. Hence, corresponding studies will be carried out to supplement our conclusions.

In conclusion, THS treatment with RFR can effectively accelerate patients' resuscitation with less infusion of resuscitation fluid, reduce mechanical ventilation time and ICU stay, as well as promote coagulation recovery. RFR has better effects and is suitable for clinical application.

Disclosure of conflict of interest

None.

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