

## Original Article

# Restricted fluid resuscitation improves the prognosis of patients with traumatic hemorrhagic shock

Xingsheng Gu, Shuguang Wang, Jia'nan Chen, Feng Cao, Li Zhou

Department of Emergency, Ningbo No. 6 Hospital, Ningbo, Zhejiang Province, China

Received April 16, 2020; Accepted May 22, 2020; Epub July 15, 2020; Published July 30, 2020

**Abstract:** Objective: To explore the effect of restricted fluid resuscitation on coagulation, the serum inflammatory factors, and the prognoses of patients with traumatic hemorrhagic shock. Methods: This prospective randomized controlled trial recruited 160 patients with traumatic hemorrhagic shock from the Department of Emergency in Ningbo No. 6 Hospital. The patients were randomly divided into two groups: the patients in one group received restricted fluid resuscitation (the experimental group, n=80) and the patients in the other group received routine fluid resuscitation (the control group, n=80). The differences in the infusion volumes and mean arterial pressure (MAP) levels during the resuscitation as well as the levels of the serum inflammatory factors (TNF- $\alpha$ , IL-4, IL-6, IL-10) and the coagulation function indexes (platelet (PLT), prothrombin time (PT), activated partial thromboplastin time (APPT)) before and after resuscitation were compared between the two groups. The mortality and the incidences of acute respiratory distress syndrome (ARDS) and multiple organ dysfunction syndrome (MODS) of the patients in both groups during their hospital stays were calculated. Results: During the fluid resuscitation, the infusion volume in the experimental group was significantly lower than it was in the control group ( $P<0.001$ ). After the resuscitation, the experimental group had significantly lower MAP and serum TNF- $\alpha$ , IL-4, IL-6 and IL-10 levels, but significantly higher plasma lactic acid, hemoglobin (Hb), hematocrit (Hct) and base excess (BE) as well as PLT, PT, and APTT levels than the control group. The mortality (6.3% vs 16.3%,  $P=0.045$ ) and the incidences of ARDS (12.5% vs 27.5%,  $P=0.018$ ) and MODS (8.8% vs 22.5%,  $P=0.017$ ) in the experimental group were significantly lower than they were in the control group. Conclusion: Restricted fluid resuscitation can significantly improve the serum inflammatory factor levels, the coagulation indicators, and the prognoses of patients with traumatic hemorrhagic shock and can reduce their infusion volumes and MAP levels.

**Keywords:** Hemorrhagic shock, trauma, restricted fluid resuscitation, inflammatory factors, coagulation, prognosis

## Introduction

With the development of traffic and industry, especially the construction industry, traffic and fall injuries occur frequently, so trauma has become one of the most important threats to life and health in modern society [1, 2]. Research by the World Health Organization (WHO) shows that about 5.8 million people die from trauma each year. Deaths due to trauma account for about 10% of all deaths, and disabilities due to trauma account for about 16% of all disabilities [3, 4]. Research shows that trauma mainly occurs in the young and middle-aged people under 50 years old, causing severe damage to the economy and to family harmony [5]. Traumatic hemorrhagic shock is the main cause of death after trauma and accounts for

30%-40% of the deaths within 24 hours after trauma [6]. The emergency treatment of traumatic hemorrhagic shock has become a worldwide public health problem. It is of great significance to study the resuscitation strategies for traumatic hemorrhagic shock.

Traumatic hemorrhagic shock is mainly caused by excessive blood loss in the body after trauma. The dramatic decrease of the effective circulating blood volume causes a sharp decline of blood perfusion in tissues and the enhancement of anaerobic metabolism, which then leads to acute respiratory distress syndrome (ARDS) and multiple organ dysfunction syndrome (MODS) [7, 8]. Effective hemostasis and anti-shock therapy should be performed as soon as possible to prevent patients from

developing ARDS and MODS, as early prevention can greatly help avoid a poor prognosis [9]. Fluid resuscitation is an important method of anti-shock treatment for patients with traumatic hemorrhagic shock. The traditional aggressive fluid resuscitation advocates restoring the effective blood volume quickly by means of a large amount of fluid infusion. Studies have shown that aggressive fluid resuscitation can cause coagulation disorders and can increase the inflammatory factor levels [10, 11]. In recent years, restricted fluid resuscitation has become a hotspot of anti-shock therapy for patients with traumatic hemorrhagic shock. Different from the traditional aggressive fluid resuscitation, restricted fluid resuscitation advocates restoring the perfusion of vital organs and tissues with a small amount of balanced salt solution, which is also known as “permissive hypotension” [12].

However, the main focus of the research on aggressive fluid resuscitation and restricted fluid resuscitation in the past was the control of blood pressure, and there were few studies about coagulation and the serum levels of the inflammatory factors such as IL-4 and IL-10 in the patients. Therefore, the aim of our study, which was a single-center, prospective, randomized controlled trial, was to explore the effect of restricted fluid resuscitation on the prognoses of patients with traumatic hemorrhagic shock. We also studied the coagulation and inflammatory factors in patients with traumatic hemorrhagic shock after resuscitation.

### Materials and methods

#### *Patients*

This prospective randomized controlled trial recruited 160 patients with traumatic hemorrhagic shock from the Department of Emergency in Ningbo No. 6 Hospital from February 2018 to February 2020. This study was approved by the Medical Ethics Committee of Ningbo No. 6 Hospital.

Inclusion criteria: Patients who met the diagnostic criteria of hemorrhagic shock in the “Chinese emergency medicine expert consensus on diagnosis and treatment of traumatic hemorrhagic shock” issued by the Chinese College of Emergency Physicians in 2017 [13]; patients who were admitted to our hospital for

the first time and who were admitted within 6 hours of their arrival and who had not been transferred; patients who were over 18 years old; patients whose family members signed the informed consent.

Exclusion criteria: Patients who had dysfunction of the vital organs including the liver and kidneys before their admission; patients who were admitted with MODS and ARDS; patients with incomplete clinical data [14].

#### *Methods*

The patients were treated before resuscitation according to the basic principle of first aid and resuscitation [15]: first, the injury was assessed. The bleeding sites were identified quickly and appropriate medication was given to stop the bleeding. The patients were escorted to the corresponding department to perform an emergency surgical exploration for hemostasis. Because the time from shock to death is very short (about 2 h), the healthcare practitioners paid attention to the accuracy of the identification and shortened the identification and effective hemostasis times as much as possible. Second, the patients’ respiratory tracts were kept unobstructed, and continuous oxygen inhalation was maintained. A ventilator with endotracheal intubation was used when needed. Third, the vital signs were monitored. The radial artery (left or right) was catheterized and connected to a hemodynamic monitor. The patients were subjected to electrocardiographic monitoring and dynamic monitoring of their vital signs was performed. Fourth, the peripheral venous access was established and the central venous access was established as soon as possible if the conditions permitted.

The patients in the control group were treated with routine resuscitation: 1,500-2,000 mL of compound sodium chloride solution (Jilin Dubang Pharmaceutical Co., Ltd., 500 mL) was given for volume expansion. Then 500-1,000 mL of hydroxyethyl starch (Beijing Fresenius Kabi Pharmaceutical Co., Ltd., 500 mL) was given for the resuscitation.

The patients in the experimental group were treated with restricted fluid resuscitation: 500-1,500 mL of compound sodium chloride solution (Jilin Dubang Pharmaceutical Co., Ltd., 500 mL) was given within 30-60 min. Then 500 mL

of hydroxyethyl starch (Beijing Fresenius Kabi Pharmaceutical Co., Ltd., 500 mL) was given for the resuscitation. The total liquid infusion volume ranged from 1,500 mL to 2,000 mL. The mean arterial pressure (MAP) of the patients treated with routine resuscitation and restricted fluid resuscitation was kept in the range of 60-80 mmHg and 50-60 mmHg respectively. And the urine volume was maintained at more than 50 mL/h and 40 mL/h respectively [11, 12].

### *Outcome measures*

The infusion volumes of the resuscitation in both groups: The total infusion volumes of the compound sodium chloride solution and the hydroxyethyl starch were recorded.

The plasma lactic acid, Hct, and BE levels before and after the resuscitation in both groups [16]: The lactic acid plasma level was measured with a spectrophotometry kit provided by the BioVision Company. The Hct and BE plasma levels were measured with a fully automated biochemical analyzer (Manufacturer: Beckman Counter Company, Type: AU5800).

The serum levels of the inflammatory factors before and after the resuscitation in both groups [17, 18]: The TNF- $\alpha$ , IL-4, IL-6 and IL-10 serum levels were measured using the ELISA method according to the instruction of the TNF- $\alpha$  kit (Brand: Cayman, batch number: 589201-96), IL-4 kit (Brand: Abnova, batch number: ab215089), IL-6 kit (Brand: BioVision, batch number: K4143-100), IL-10 kit (Brand: Abnova, batch number: ab46034) respectively. The absorbances of the samples were measured using a Varioskan LUX multi-function microplate reader (Thermo Fisher Scientific, United States).

The coagulation indicators before and after the resuscitation in both groups [19]: The platelet count was measured using the flow fluorescence scattering method. The blood samples were collected using disposable syringes or silica glass syringes and the plasma was separated out using centrifugation. Then the time needed for plasma coagulation and the prothrombin time (PT) after adding enough thromboplastin and calcium ions into the plasma was measured. The activated partial prothrombin time (APPT) was measured using a coagulation test.

The prognoses of the patients in the two groups: The mortality and the incidences of ARDS and MODS during their hospital stays were recorded.

### *Statistical methods*

SPSS 24.0 was used for the statistical analysis. The enumeration data were expressed as n (%) and  $\chi^2$  tests and Fisher's exact tests were adopted for the comparisons between the two groups. The measurement data were expressed as the means  $\pm$  standard deviation ( $\bar{x} \pm sd$ ). Comparisons within the same group used paired-sample t-tests, and the comparisons between the two groups used independent-sample t-tests.  $P < 0.05$  (two-sided) was considered statistically significant.

## **Results**

### *Baseline data*

There were no significant differences in terms of age, sex, fluid resuscitation times, mean times from trauma to admission, shock index, injury severity scores (ISS), or the causes of the trauma in the two groups ( $P > 0.05$ , **Table 1**).

### *Comparison of the infusion volumes and the MAP levels in the two groups*

During fluid resuscitation, the infusion volume in the experimental group was significantly lower than it was in the control group ( $1526.4 \pm 115.7$  mL vs  $2754.9 \pm 153.8$  mL,  $P < 0.001$ ). See **Figure 1A**. There was no significant difference in the MAP levels in the two groups at the time of admission ( $59.3 \pm 6.3$  mmHg vs  $58.6 \pm 6.9$  mmHg,  $P = 0.222$ ). Compared with the levels at admission, the MAP levels in the control group increased significantly after the resuscitation ( $P < 0.001$ ), but in the experimental group the levels didn't change significantly after the resuscitation ( $P > 0.05$ ). After the resuscitation, the MAP levels in the experimental group were significantly lower than the levels in the control group ( $61.3 \pm 3.5$  mmHg vs  $71.1 \pm 4.6$  mmHg,  $P < 0.001$ ). See **Figure 1B**.

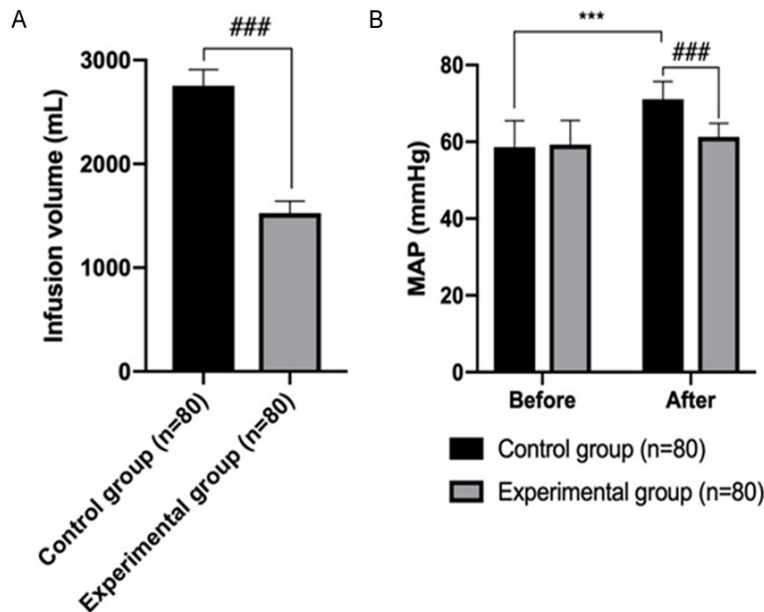
### *Comparison of the lactic acid, Hct, and BE plasma levels in the two groups*

Before the resuscitation, there was no significant difference in the lactic acid, Hb, Hct, or BE levels in the two groups ( $P < 0.05$ ). After the

**Table 1.** Baseline information (n (%))/( $\bar{x} \pm sd$ )

Items	Control group (n=80)	Experimental group (n=80)	$\chi^2/t$	P
Age (year)	38.1 $\pm$ 8.7	36.8 $\pm$ 7.5	1.012	0.313
Gender (male/female, n (%))	53 (66.3)/27 (34.7)	59 (73.8)/21 (26.2)	1.071	0.301
BMI (kg/m <sup>2</sup> )	23.8 $\pm$ 2.9	23.3 $\pm$ 3.2	1.036	0.302
Time for fluid resuscitation (h)	1.5 $\pm$ 0.3	1.6 $\pm$ 0.4	1.789	0.076
Time from injury to admission (h)	2.3 $\pm$ 1.3	2.5 $\pm$ 1.5	0.901	0.369
Shock index	2.2 $\pm$ 0.4	2.1 $\pm$ 0.4	1.581	0.116
ISS (score)	28.3 $\pm$ 2.9	27.6 $\pm$ 3.2	1.450	0.149
Cause of injury (n, %)				
Traffic injury	48 (60.0)	51 (63.8)	0.120	0.793
Fall injury	12 (15.0)	10 (12.5)		
Smashed injury	10 (12.5)	11 (13.8)		
Crush injury	7 (8.8)	7 (8.8)		
Others	3 (3.8)	1 (1.3)		

Note: BMI: body mass index; ISS: injury severity score.



**Figure 1.** Comparison of the infusion volume and MAP levels in the two groups. A: Infusion volume during the resuscitation in both groups; B: MAP before and after the resuscitation in both groups. Compared with the control group before the resuscitation, \*\*\* $P < 0.001$ ; compared with the control group, ### $P < 0.001$ . MAP: mean artery pressure.

resuscitation, the lactic acid, HB, and Hct levels in both groups all decreased significantly ( $P < 0.001$ ), but the BE plasma levels in both groups increased significantly ( $P < 0.001$ ). Compared with the control group, the lactic acid, HB, Hct, and BE levels were significantly higher in the experimental group after the resuscitation ( $P < 0.001$ ). See **Table 2**.

#### Comparison of serum levels of inflammatory factors between the two groups

Before the resuscitation, there were no significant difference in the TNF- $\alpha$ , IL-4, IL-6, or IL-10 serum levels in the two groups ( $P > 0.05$ ). After the resuscitation, the inflammatory factor levels in the two groups all significantly increased ( $P < 0.001$ ), and the levels of these inflammatory factors in the experimental group were significantly lower than those in the control group ( $P < 0.001$ ). See **Table 3**.

#### Comparison of the coagulation in the two groups

Before the resuscitation, there were no significant differences in the coagulation indicators (PLT, PT, and APTT) in the two groups ( $P > 0.05$ ).

Compared with the PT at admission, the PT in the control group didn't change significantly after the resuscitation ( $P > 0.05$ ), but it was significantly increased in the experimental group ( $P < 0.001$ ). The PLT, PT, and APTT levels in the experimental group were significantly higher than they were in the control group after the resuscitation ( $P < 0.05$ ). See **Table 4**.

**Table 2.** Comparison of the lactic acid, Hct, and BE serum levels before and after the resuscitation in both groups

Items	Lactic acid (mmol/L)	Hb (g/L)	Hct	BE (mmol/L)
Control group (n=80)				
Before resuscitation	4.7±1.5	121.9±14.9	0.34±0.06	-10.5±3.7
After resuscitation	2.2±1.0	92.8±10.7	0.23±0.09	-6.5±2.2
t	5.289	14.189	9.096	8.311
P	<0.001	<0.001	<0.001	<0.001
Experimental group (n=80)				
Before resuscitation	5.1±1.6	123.7±13.8	0.36±0.08	-11.3±4.5
After resuscitation	3.6±1.1 <sup>###</sup>	114.5±9.3 <sup>###</sup>	0.30±0.07 <sup>###</sup>	-4.3±1.8 <sup>###</sup>
t	13.74	4.945	5.048	12.918
P	<0.001	<0.001	<0.001	<0.001

Note: Compared with the control group after the resuscitation, <sup>###</sup>P<0.001. Hb: hemoglobin; HCT: hematocrit; BE: base excess.

**Table 3.** Comparison of the inflammatory factor serum levels before and after the resuscitation

Items	TNF-α (pg/mL)	IL-4 (pg/mL)	IL-6 (pg/mL)	IL-10 (pg/mL)
Control group (n=80)				
Before resuscitation	67.8±8.7	485.9±54.3	162.5±18.2	332.9±36.7
After resuscitation	124.7±11.3	759.9±82.3	251.5±20.7	520.3±43.9
t	35.686	24.856	28.881	29.293
P	<0.001	<0.001	<0.001	<0.001
Experimental group (n=80)				
Before resuscitation	69.5±9.2	477.9±51.7	166.3±17.8	320.4±40.3
After resuscitation	82.5±10.1 <sup>###</sup>	633.2±67.9 <sup>###</sup>	210.6±14.9 <sup>###</sup>	432.7±38.7 <sup>###</sup>
t	8.511	16.276	17.069	17.977
P	<0.001	<0.001	<0.001	<0.001

Note: Compared with the control group after the resuscitation, <sup>###</sup>P<0.001. TNF-α: tumor necrosis factor α; IL-4: interleukin 4; IL-6: interleukin 6; IL-10: interleukin 10.

### Comparison of the prognoses in the two groups

The incidences of death (6.3% vs 16.3%, P=0.045), ARDS (12.5% vs 27.5%, P=0.018), and MODS (8.8% vs 22.5%, P=0.017) in the experimental group were all significantly lower than those in the control group respectively. See Table 5.

### Discussion

The rapid decrease of blood volume is the cause of traumatic hemorrhagic shock, and the hypoperfusion of vital organs and surrounding tissues is the key to the progression of the disease, which has five characteristics. First, changes in microcirculation [20]: catecholamine-mediated arteriolar contraction after massive blood loss leads to a decreased perfusion pressure of the microcirculation and the

cytotoxic edema, which can promote the contraction of the capillaries; finally, these effects will aggravate the decreased perfusion of the microcirculation and lead to a “waterfall effect”. Second, changes in cell metabolism [21]: when the oxygen-carrying capacity of blood cells and effective blood volume cannot meet the metabolic requirements of tissues, the anaerobic metabolism of the cells is enhanced, leading to high plasma levels of lactic acid and finally inducing metabolic acidosis; with the aggravation of the oxygen debt, cell membrane rupture, cell apoptosis, or necrosis will occur due to the disruptions in cellular homeostasis. Third, changes in the inflammatory factor concentrations [22]: the body produces and releases a large amount of inflammatory mediators such as TNF-α after a massive blood loss caused by trauma. The body's anti-inflammatory capacity increases as the disease progresses. Meanwhile, IL-4, IL-6, IL-10, and other inflammatory



**Table 4.** Comparison of coagulation indicators before and after the resuscitation

Items	PLT ( $\times 10^9/L$ )	PT (second)	APPT (second)
Control group (n=80)			
Before resuscitation	33.5 $\pm$ 9.5	32.8 $\pm$ 3.3	104.7 $\pm$ 18.6
After resuscitation	38.7 $\pm$ 7.2	33.3 $\pm$ 4.6	111.1 $\pm$ 19.2
t	3.902	0.79	2.141
P	0.001	0.431	0.034
Experimental group (n=80)			
Before resuscitation	34.3 $\pm$ 9.2	31.7 $\pm$ 4.3	106.8 $\pm$ 20.7
After resuscitation	48.7 $\pm$ 5.5 <sup>###</sup>	34.9 $\pm$ 4.9 <sup>#</sup>	125.6 $\pm$ 20.2 <sup>###</sup>
t	12.016	4.39	5.814
P	<0.001	<0.001	<0.001

Note: Compared with the control group after the resuscitation, <sup>#</sup>P<0.05, <sup>###</sup>P<0.001. PLT: platelet; PT: prothrombin time; APPT: activated partial thromboplastin time.

**Table 5.** Comparison of the prognosis

Items	Control group (n=80)	Experimental group (n=80)	$\chi^2$	P
Death	13 (16.3)	5 (6.3)	4.006	0.045
ARDS	22 (27.5)	10 (12.5)	5.625	0.018
MODS	18 (22.5)	7 (8.8)	5.736	0.017

Note: ARDS: acute respiratory distress syndrome; MODS: multiple organ dysfunction syndrome.

factors are synthesized and released. The inflammatory factors induce the expression of adhesion molecules on the surface of the endothelium, which promotes the adhesion and rolling of activated white blood cells, thus causing irreversible damage to the cells and terminal organs. Fourth, changes in coagulation [23]: after trauma, the body can reduce the level of fibrinogen by activating the protein C system, which causes dysfunctional anticoagulation and fibrinolysis. A large amount of activated thrombin can further induce diffuse coagulopathy. Fifth, multiple organ dysfunction syndrome [24]: the hypoperfusion of organs and tissues can cause cell degeneration in the liver, kidneys, and other tissues. The dysfunction of inflammatory factors and coagulation can aggravate organ function damage. All these factors can eventually lead to multiple organ dysfunction and even organ failure. Therefore, traumatic hemorrhagic shock is a serious injury to multiple systems of the body. During anti-shock treatment, the medical staff should pay close attention to changes in microcirculation, cell metabolism, the inflammatory factors, coagulation, and organ function.

Maintaining stable hemodynamics is an important measure for the treatment of hemorrhagic shock, and it can effectively correct the insufficiency of tissue perfusion pressure and cell metabolism disorder. Therefore, the traditional fluid resuscitation treatment advocates restoring patients' blood pressure to normal as soon as possible. However, the short-term ischemia-reperfusion of tissues will further aggravate the tissue damage [25, 26]. Matlox et al. proposed the concept of delayed resuscitation in 1996, which denied the rationality of rapid fluid resuscitation. They stated that blood pressure should be restored to a level sufficient to maintain vital tissues and organs first, then to a normal level. This method can reduce tissue damage and

improve prognosis [27]. At present, the liquid resuscitation method is still controversial in the clinic, and the outcome measures on the effect of liquid resuscitation in most previous studies are not satisfactory. In our study, several representative indicators were selected to evaluate the effect of traditional aggressive fluid resuscitation and restricted fluid resuscitation on traumatic hemorrhagic shock. The MAP levels before and after resuscitation were measured to evaluate the recovery of tissues with perfusion. The plasma lactic acid, Hct, and BE levels were measured to determine the anaerobic metabolism of the tissue cells. The serum TNF- $\alpha$ , IL-4, IL-6, and IL-10 levels were measured to evaluate the inflammatory factor levels. The plasma PLT, PT, APTT levels were measured to estimate the coagulation. We used comprehensive indicators to evaluate the effect of resuscitation, which was rarely done in previous studies.

Low infusion volumes and low MAP levels are the main characteristics of restricted fluid resuscitation. Accordingly, in our study we used relatively small amounts of fluid to restore relatively low MAP levels in the experimental group.

The infusion volume and MAP level results in our study are consistent with those reported by Kudo et al. and Carrick et al. [28]. Meanwhile, there was no significant difference in the baseline MAP levels in the two groups before resuscitation, but the MAP levels all increased significantly in both groups after resuscitation. The reason may be that fluid resuscitation expands the volume of the circulatory system and increases the effective circulating blood volume, which then increases the MAP levels. However, the MAP levels in the experimental group were significantly lower than they were in the control group. And the results are consistent with those reported by Carrick et al. [29].

The results of our study showed that the effect of restricted fluid resuscitation on improving the cellular anaerobic metabolism and coagulation and alleviating the release of inflammatory factors were better than traditional fluid resuscitation. The serum lactic acid, HB, Hct, and BE levels were measured to observe the anaerobic metabolism of the cells. The lactic acid, HB, Hct, and BE levels in both groups all decreased significantly after the resuscitation, and the decline of the restricted fluid resuscitation was more dramatic, which is consistent with the results reported by Ho et al. [30]. The TNF- $\alpha$ , IL-4, IL-6, and IL-10 serum levels in both groups all increased significantly after the resuscitation, but the increase of the restricted fluid resuscitation was smaller than the increase of the traditional fluid resuscitation. The reason may be that restricted fluid resuscitation is more effective in alleviating the elevated levels of the inflammatory mediators caused by tissue reperfusion. Because the patients synthesized a large amount of the inflammatory mediators before the resuscitation, the total level still increased significantly after the resuscitation [31, 32]. The PLT, PT, and APPT levels in the two groups all changed after the fluid resuscitation, but the changes in the experimental group were more significant, which indicated that restricted fluid resuscitation can restore the coagulation function more effectively. These results are similar to the research reported by Rasheed et al. [33].

We also found that the mortality and incidences of ARDS and MODS in the patients with restricted fluid resuscitation were significantly

lower than those with traditional aggressive fluid resuscitation, indicating that the effect of restricted fluid resuscitation not only significantly changes the microcirculation, cell metabolism, inflammatory factor levels, and coagulation it also improves the prognoses of patients better than traditional fluid resuscitation. Xiao et al. performed restricted fluid resuscitation on 219 patients with traumatic shock, and they found the incidences of ARDS and MODS were 18.3% and 17.4%, respectively [34], incidences slightly higher than the results in our study. But the mortality (9.13%) was similar to what we observed in our study.

There are still some limitations to our study. Firstly, we only recruited patients with traumatic hemorrhagic shock, so the effects of restricted fluid resuscitation in patients with other types of shock are unclear. Moreover, because of the great differences in the treatments of patients with traumatic hemorrhagic shock, our study only observed the related outcome measures before and after the resuscitation, and we did not follow up with subsequent clinical data. Furthermore, the target level of the MAP of restricted fluid resuscitation is another hotspot of current research; however, we did not study the effect of restricted fluid resuscitation with different MAP levels on patients with other types of shock.

In conclusion, restricted fluid resuscitation has a higher application value in patients with traumatic hemorrhagic shock. It not only improves patients' microcirculation and coagulation functions, it also effectively alleviates the anaerobic metabolism of tissue cells and the release of the inflammatory factors. Compared with traditional aggressive fluid resuscitation, restricted fluid resuscitation can improve patient prognosis, effectively reducing the mortality and decreasing the incidences of ARDS and MODS.

### Disclosure of conflict of interest

None.

**Address correspondence to:** Li Zhou, Department of Emergency, Ningbo No. 6 Hospital, No. 1059 Zhongshan East Road, Ningbo 315040, Zhejiang Province, China. Tel: +86-18906627957; E-mail: zhouli7c3a@163.com

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