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## Fluid resuscitation of trauma patients: How much fluid is enough to determine the patient's response?

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### 1. Introduction

The topic of damage control resuscitation has become increasingly popular during the last several years [1–4]. This topic involves several key concepts that include permissive hypotension (restrictive fluid resuscitation), which is a strategy that restricts fluid use before any bleeding is controlled to avoid excessive blood loss. However, the related studies have mainly evaluated patients with penetrating injury and in the pre-hospital setting. Therefore, it is unclear whether this approach provides benefits in cases of blunt trauma or in-hospital setting. In addition, patients with hypotension should be rapidly stabilized with a moderate fluid infusion to maintain tissue perfusion. Therefore, the American College of Surgeon's Advanced Trauma Life Support training program emphasizes a “balanced” approach to ensure adequate tissue perfusion and minimize the risk of re-bleeding by avoiding inadequate or excessive fluid administration [5].

The Advanced Trauma Life Support and Japan Advanced Trauma Evaluation and Care guidelines both recommend an initial rapid infusion of fluid (1–2 L) as a diagnostic procedure for patients who have experienced trauma or hemorrhage [5,6]. However, the appropriate volume of fluid infusion has not been clearly defined, despite the patient's responses to the initial fluid resuscitation being critical to selecting an appropriate therapeutic strategy. Therefore, this study aimed to determine the optimal volume of fluid infusion during the initial resuscitation of patients who had experienced trauma and hypotension.

### 2. Methods

This prospective descriptive 3-year study (2008–2011) evaluated ≥ 16-year-old patients with blunt trauma and a systolic blood pressure (SBP) of ≤90 mm Hg at admission. We excluded patients who had received any fluids before the admission, such as patients who had been transferred from other hospitals. The standard trauma resuscitation protocols were used for all other components of care. The patients' hemodynamic parameters were recorded after 1 L and 2 L of fluid resuscitation. Institutional review board (Rinku General Medical Center) approved the study. Non-response (hemodynamic instability) was defined as sustained hypotension (SBP of ≤90 mm Hg) or prolonged tachycardia (heart rate [HR] of >120 bpm) after 1 L and 2 L of fluid resuscitation. All uses of surgery or interventional radiology to control hemorrhage were reviewed and reevaluated. We also evaluated the abilities of non-response and SBP after 1 L and 2 L of fluid resuscitation to predict the requirement for an immediate intervention using receiver operating characteristic curve analysis. All data were presented as mean ± standard deviation.

### 3. Results

We enrolled 69 patients, who had an average age of 50.3 ± 20.7 years and an average injury severity score of 29.9 ± 13.9. Thirty-nine patients required an intervention, and 30 patients did not require an intervention for control hemorrhage. The sites of hemorrhage for the cases that required an intervention were pleural hemorrhage ( $n = 3$ ), peritoneal hemorrhage ( $n = 12$ ), retroperitoneal hemorrhage ( $n = 19$ ), and other sites ( $n = 6$ ). The overall mortality rate was 23.2%. Thirteen patients in the IV groups died because of hemorrhagic shock. The sites of hemorrhage in these patients were the pleura ( $n = 3$ ), peritoneum ( $n = 4$ ), and retroperitoneum ( $n = 6$ ). All sources of bleeding

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**Table 1**  
Characteristics of the study patients.

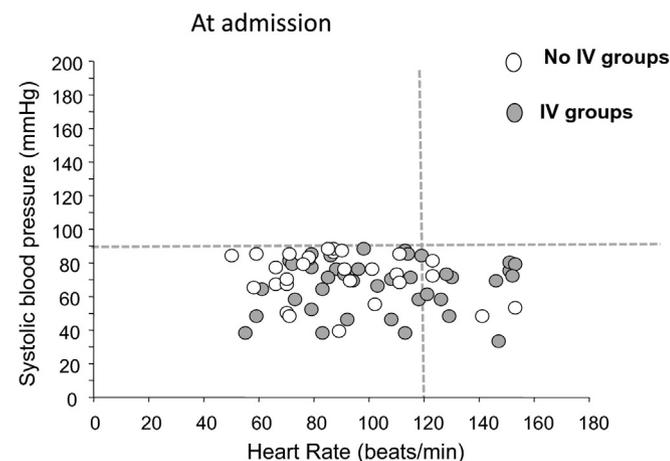
	IV groups	No IV groups	p
No. of patients	40	29	
Age (y)	47.1 ± 21.3	54.6 ± 19.4	0.52
Initial SBP (mmHg)	69.1 ± 15.0	73.1 ± 14.6	0.93
ISS	34.3 ± 14.1	24.4 ± 11.8	0.53
RTS	5.23 ± 1.68	5.32 ± 1.91	0.27
TRISS	0.61 ± 0.35	0.66 ± 0.37	0.28
Mortality	13 (32.5%)	3 (10.3%)	< 0.01

IV, intervention; SBP, systolic blood pressure; ISS, Injury Severity Score; RTS, Revised Trauma Score.

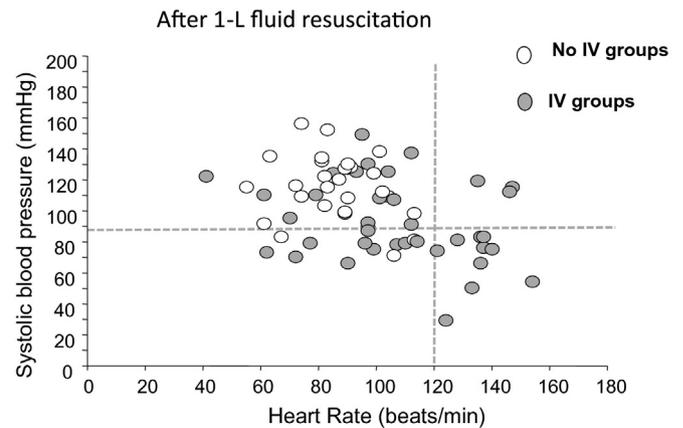
were confirmed by surgical intervention. However, three patients died in the no IV groups because of severe brain damage. The overall mortality rate was 23.2%. The group that required an intervention exhibited a non-significantly higher injury severity score, compared to the group that did not require an intervention (Table 1).

Among the 69 patients, 27 patients remained hemodynamically unstable after 1 L of fluid resuscitation, and 23 of these patients required an immediate intervention. After 1 L of resuscitation, the intervention group exhibited a higher frequency of tachycardia with a depressed SBP (Figs. 1, 2). The average fluid rate for the 1-L resuscitation was 64 ± 28 mL/min. Forty-two patients were hemodynamically stable after 1 L of fluid resuscitation, 17 of these patients required an intervention for bleeding, and 25 of these patients did not require an intervention. Non-response after 1 L of fluid resuscitation provided a positive predictive value of 86.3% for predicting intervention, and a negative predictive value of 59.5% for predicting no intervention.

Fifty-eight patients received 2 L of fluid resuscitation, 20 of these patients remained hemodynamically unstable, and 16 of these patients required an intervention. Some patients responded to the 2 L of fluid and intervention with a restored SBP and decreased HR (Fig. 3). The average fluid rate for the 2-L resuscitation was 62.0 ± 29.0 mL/min. Non-response after 2 L of fluid resuscitation provided a predictive value of 80.0% for predicting intervention, which was lower than the positive predictive value of non-response after 1 L of fluid resuscitation. Thirty-eight patients were hemodynamically stable after 2 L of fluid resuscitation, 16 of these patients required an intervention for bleeding, and 20 of these patients did not require an intervention. The negative predictive value was 52.6% for predicting no intervention, and this value was also lower than the value for 1 L of fluid resuscitation.



**Fig. 1.** Systolic blood pressure (SBP) and heart rate (HR) at admission. Closed circles: patients who required immediate interventions for bleeding. Open circles: patients who required no interventions.



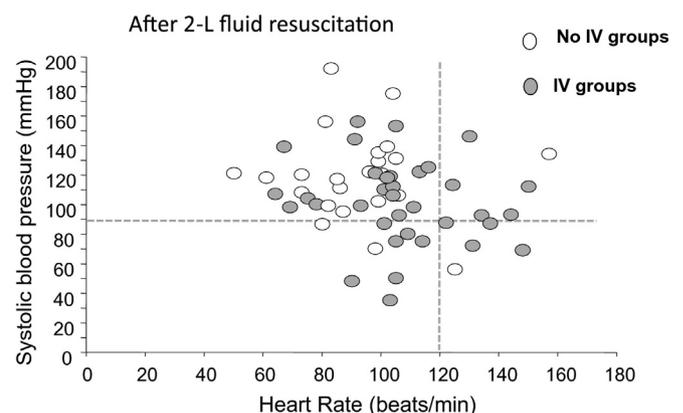
**Fig. 2.** Systolic blood pressure (SBP) and heart rate (HR) after 1-L fluid resuscitation. The average fluid rate was 64 mL/min. Non-response to resuscitation was defined as sustained hypotension (SBP of <90 mm Hg) or prolonged tachycardia (HR of >120 bpm). Non-response after 1-L fluid resuscitation had a positive predictive value of 86.3% for intervention and a negative predicting value of 59.5% for no intervention.

The areas under the receiver operating characteristic curves for SBP were 0.61 (at admission), 0.72 (after 1 L of fluid resuscitation), and 0.68 (after 2 L of fluid resuscitation) (Fig. 4).

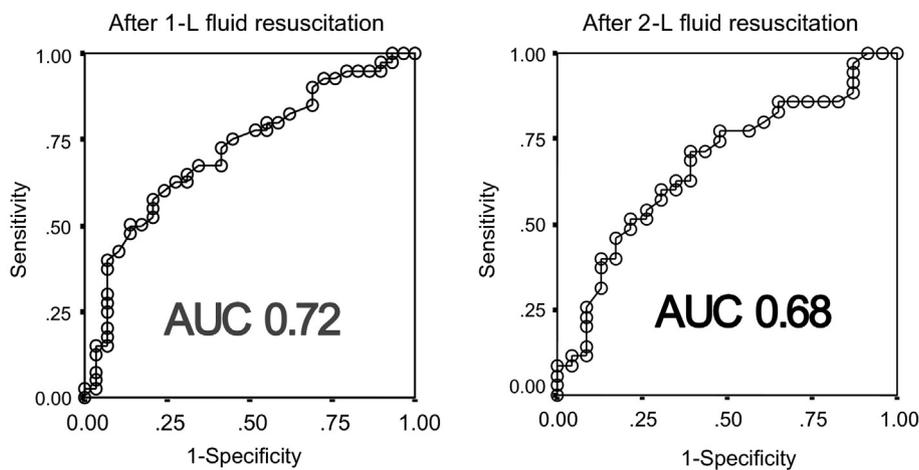
#### 4. Discussion

The basic principles of trauma management are to stop bleeding and replace the lost volume. Thus, fluid resuscitation can be used to assess the patient's response and provide evidence of adequate end-organ perfusion and oxygenation. In this context, the patient's response is observed during the initial fluid administration, and further therapeutic and diagnostic decisions are based on this response [5,6]. There are three generally accepted types of response to fluid resuscitation (rapid response, transient response, and non-response), and non-responders do not exhibit hemodynamic improvement after fluid administration, because of their ongoing hemorrhage. Therefore, non-response to crystalloid and blood administration indicates the need for an immediate and definitive intervention (instead of simple volume replacement) to control the hemorrhage and delays in implementing definitive management can be lethal.

An increasing body of evidence has recently revealed that intravenous fluid administration does not improve survival in cases of trauma, and may actually be harmful in certain cases [1,2]. This is because fluid resuscitation and the avoidance of blood pressure elevation can



**Fig. 3.** Systolic blood pressure (SBP) and heart rate (HR) after 2-L fluid resuscitation. The average fluid rate was 61 mL/min. Non-response after 2-L fluid resuscitation had a predictive value of 80.0% for intervention and a negative predicting value of 52.6% for no intervention.



**Fig. 4.** Receiver operating characteristics (ROC) curve for systolic blood pressure (SBP) after 1-L and 2-L fluid resuscitation to predict intervention. The area under the ROC curve was 0.72 after 1-L fluid resuscitation, and the area under the ROC curve was 0.68 after 2-L fluid resuscitation.

potentially displace established clots and cause hemorrhage recurrence. Thus, there is a strong argument that excessive fluid administration may aggravate any organ failure, and that additional fluid should not be administered except to correct hypotension. Nevertheless, most studies of restricted fluid resuscitation evaluated cases with penetrating injuries, and it is easy to identify the site(s) of bleeding in these cases [4,8]. Thus, it may be more difficult to identify cases of blunt trauma that require surgical interventions based on vital signs at admission, and the patient's response to fluid resuscitation is critical to determining the subsequent therapy. Moreover, in the present study, 30 of the 69 patients (43%) who had experienced trauma and hypotension did not require any interventions for bleeding.

Few reports have described the initial fluid resuscitation volume and rate, although one study used propensity analysis to control for group differences and concluded that >500 mL of fluid corrected hypotension and improved the mortality rate among patients with pre-hospital hypotension [3]. Thus, most studies of restricted fluid strategies have been performed in the pre-hospital setting. Furthermore, Schreiber et al. performed a randomized study of controlled resuscitation (mean crystalloid volume: 1 L) and standard resuscitation (mean crystalloid volume: 2 L), which revealed that the controlled resuscitation strategy was feasible and safe among hypotensive trauma patients in the pre-hospital and in-hospital settings [7]. These findings indicate that a moderate resuscitation volume may be appropriate for these patients in the pre-hospital and in-hospital settings.

Ley et al. have also demonstrated that  $\geq 1.5$  L of emergency crystalloid fluid resuscitation was an independent risk factor for mortality among elderly and non-elderly patients who had experienced trauma [9], which indicates that an emergency intervention or a rapid intensive care unit admission should be considered if  $\geq 1.5$  L of fluid is required to maintain adequate blood pressure [9]. Moreover, Hagiwara et al. have reported that a shock index of  $\geq 1$  after 1 L of resuscitation was assigned to patients who required a blood transfusion or intervention for active bleeding [10]. Thus, low-volume fluid resuscitation appears to have competing benefits (identification of the patient's response after blunt trauma) and risks (reduced tissue perfusion among patients with shock who respond to fluid). Therefore, it appears that a moderate fluid infusion rate and volume should be considered to evaluate the patient's response to fluid resuscitation.

Our previous study demonstrated that increasing the fluid administration rate (to >60 mL/min) did not produce hemodynamic stability, and that more aggressive fluid resuscitation rates may result in excessive fluid resuscitation [11]. Therefore, the present study used a moderate rate that is approximately equal to the rate that is provided by a fully-open 16-G peripheral intravenous catheter.

Our results indicate that non-response after 1 L of fluid resuscitation provided a better ability to predict the need for intervention, compared to non-response after 2 L of fluid resuscitation. Furthermore, the receiver operating characteristic curve for SBP provided the highest value after 1 L of fluid resuscitation (vs. at admission or after 2 L of fluid resuscitation). Therefore, it might be more appropriate to evaluate patient response after 1 L of fluid administration (vs. after 2 L) to assess the need for an intervention to stop bleeding.

The findings of this study are limited by the single-center design and small sample size. Thus, large multicenter studies are needed to confirm these preliminary results, and to evaluate the utility of 1-L fluid resuscitation. Nevertheless, fluid resuscitation at a moderate rate and volume may help provide better identification of patients who require immediate interventions.

## 5. Conclusions

Our findings show that increasing the fluid administration volume did not provide a better ability to predict the need for intervention. Moderate fluid resuscitation should be considered to determine patients' response to the initial fluid resuscitation in trauma patients.

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