Original Article

Fluid resuscitation based on pulse contour cardiac output monitoring is associated with improved prognosis in adult severe burn patients: a retrospective cohort study

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Background: A monitoring method is needed to further guide fluid resuscitation in severe burn injury. This study was performed to investigate the effects of pulse contour cardiac output (PCCO) monitoring on the prognosis of adult severe burns patients.

Methods: We conducted a retrospective study enrolling patients from January 2015 to December 2020, who were divided into a control group receiving conventional monitoring and a study group receiving PCCO monitoring. The primary outcomes were 28-day mortality and total mortality, and the secondary outcomes included burn-related complications and the length of hospital stay and ICU stay. Multivariable logistic regression analysis and linear regression analysis were performed to determine the risk factors of burns-related complications and length of hospital stay in enrolled patients.

Results: A total of 109 patients in the control group and 82 patients in the study group were enrolled. While the area of full thickness burn was much higher in the control group than in the study group (P=0.021), no significant difference was found in other characteristics between the two groups. During fluid resuscitation, the fluid volume ratio of the study group was significantly different from that of the control group, and both in the first 24 hours and the second 24 hours, the resuscitation fluid volume ratio and colloid volume ratio was significantly higher in the control group than in the study group (all P<0.001). Eight patients died during treatment, and there were more patients experiencing AKI and ARDS in the control group than in the study group (P=0.029 and 0.016). The lengths of hospital stay and ICU stay in the study group was much shorter than in the control group (P<0.001 and 0.005). In addition, TBSA was an important risk factor for both AKI and ARDS, and the existence of inhalation injury and older age increased the incidence of ARDS. Higher TBSA, inhalation injury, and burn-related complications were related to longer hospital stay in enrolled patients.

Conclusions: Fluid resuscitation according to PCCO monitoring can effectively reduce the volume of colloid and overall fluid volume and reduce the incidence of burns-related complications and shorten the length of hospital stay.

Keywords: Fluid resuscitation; pulse contour cardiac output monitoring (PCCO monitoring); improved prognosis; severe burn; a retrospective cohort study

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Introduction

Acute burn injury is a very common form of trauma, with high rates of morbidity and mortality. In China, it has been reported that about 26 million people suffer from different degrees of burns and scalds every year (1), and globally, burns can cause about 330,000 deaths each year (2). In cases of severe burns, the homeostasis of the body will be disrupted due to stress reactions and subsequent infection. Multiple types of inflammatory related factors are released from immune cells, resulting in increased capillary permeability (3), and a large amount of body fluids will be transferred from the blood vessel to the intercellular space, resulting in insufficient volume of circulating blood. Therefore, burns patients are very prone to hypovolemia and shock (4), which can lead to organ dysfunction or failure, such as acute kidney injury (AKI) and acute respiratory distress syndrome (ARDS). It has been reported that about 30% of major burns patients have AKI as well as ARDS during the period of fluid resuscitation, and the occurrence of AKI and ALI further worsens patient outcomes (5,6).

Timely fluid resuscitation is very important for the treatment of severe burns patients, especially within the first 8 to 24 hours (7). However, there is a lack of unified fluid resuscitation formulas and protocols, and controversy remains as to how this should be conducted. While common fluid resuscitation formulas used globally include modified parkland, modified Brooke, Evans, Muir Barclay, and Haifa formula (8), in recent years, the formula of the Third Military Medical University (TMMU) has been widely applied in China (9). Most formulas currently used are crystalloid-based, which can obtain certain curative effect, although there are some differences in their mechanism and effect (10). While current liquid resuscitation formulas mostly focus on the initial stage of liquid resuscitation, it may be inappropriate to perform this according to any one formula in the later stage of severe burns. Insufficient fluid will aggravate hypovolemic shock and organ failure, and excessive fluid will also increase the incidence of infection complications (11,12). Therefore, a monitoring method is required to further guide fluid resuscitation in the late stage of severe burns.

Cardiac output (CO) is usually monitored by pulmonary artery thermodilution using a pulmonary artery catheter to assess hemodynamic instability in critically ill patients, including severe burns patients (13). However, the safety of pulmonary artery catheterization is still controversial, and less invasive methods for CO monitoring are yet to be fully developed. Pulse contour cardiac output (PCCO) analysis is a new minimally invasive technique which has emerged in recent decades (14). The single thermal indicator technique is used in PCCO to calculate volumetric parameters of CO using a modified Wesseling algorithm (15), and has been beneficial to patients with acute and chronic heart failure and constrictive pericarditis (16-18). However, there are no related studies investigating the effects of PCCO monitoring on the prognosis of adult severe burns patients.

Therefore, we performed this single center retrospective study to analyze the effects of PCCO monitoring on the prognosis of adult patients with severe burns using multivariable logistic regression. It was hypothesized that the application of PCCO monitoring would decrease total mortality and the incidence of burn-related complications in severe burns patients and may also shorten the length of hospital stay. We present the following article in accordance with the STROBE reporting checklist (available at https://dx.doi.org/10.21037/apm-21-2587).

Methods

Patients and study design

This was a retrospective study performed in a single center of the Affiliated Hospital of Jiangnan University enrolling patients from January 2015 to December 2020. The inclusion criteria were as follows: patients older than 18 years and younger than 80 years, admitted to our hospital within 8 hours after burn injury, with a total burn surface area (TBSA) larger than 40%, and without life-threatening comorbid diseases. The exclusion criteria were as follows: patients who died within 24 hours after admission, those given palliative comfort care only, and those without complete data. Based on the treatment pattern they received, enrolled patients were divided into a control group receiving fluid resuscitation and conventional monitoring, and a study group receiving fluid resuscitation and PCCO monitoring. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by institutional ethics committee of Affiliated Hospital of Jiangnan University (No. 2021011). Individual consent for this retrospective analysis was waived.

Fluid resuscitation protocol

Fluid resuscitation was performed in enrolled patients

according to the TMMU formula (19). In detail, the volume of fluid given in the first 24 hours was calculated as 1.5 mL/kg/% TBSA + 2,000 mL, and 0.75 mL/kg/% TBSA +2,000 mL of fluid was then given in the second 24 hours. Lactated Ringer's solution was the first choice of crystalloid and frozen plasma or 5% albumin solution was selected as the colloid, with a ratio of crystalloid to colloid of 2:1. An extra 2,000 mL of 5% glucose solution was used as the basic requirement of the body for water. After this, the strategy of fluid resuscitation in the control group was adjusted according to clinical parameters during the treatment, including heart rate, blood pressure, urine volume, respiratory rate, and SpO_2, while PCCO provided some additional clinical parameters in the study group, including global end-diastolic volume index, intrathoracic blood volume index, cardiac index, system vascular resistance index, and extravascular lung water index, which were also used to adjust the fluid resuscitation strategy.

Data collection

The demographic and clinical data of patients in the two groups collected at admission were as follows: age, sex, body weight, etiology of burn injury, TBSA, area of full thickness burn, inhalation injury, time to resuscitation, and chronic comorbid diseases. Baseline data of urine output, serum creatinine (sCr), blood urea nitrogen (BUN), creatine kinase-MB (CK-MB), and procalcitonin (PCT) were also collected. Resuscitation fluid volume ratio, crystalloid volume ratio, and colloid volume ratio (mL/kg/% TBSA) in the first and second 24 hours postburn were then collected in both groups.

Outcome measurements and definitions

The primary outcomes in this study were 28-day mortality and total mortality of enrolled patients, while the secondary outcomes included burn-related complications, such as AKI, ARDS, sepsis, and venous thromboembolism, and the length of hospital stay and ICU stay. The incidence of AKI was defined as an increase in sCr of at least 26.4 μmol/L over the baseline, or an increase in sCr of at least two-fold over the baseline. The incidence of ARDS was defined according to the Berlin definition (20).

Statistical analysis

All statistical analysis was performed using SPSS 18.0 (IBM corporation, NY, USA). Continuous variables were expressed by mean with standard deviation and compared by *t*-test, and binary variables were expressed by number with percentage and compared using chi-square test. Multivariable logistic regression analysis was performed to determine the risk factors of mortality and burn-related complications in enrolled patients, and multivariable linear regression analysis was performed to investigate the relationship between the use of PCCO monitoring and length of hospital stay. P values less than 0.05 were considered statistically significant.

Results

More than 550 patients were admitted to our hospital due to burn injury between January 2015 and December 2020. Of these, 320 were diagnosed as having severe burns and 5218 patients were excluded. A further 129 patients were excluded due to incomplete data and early death, and 191 patients were finally enrolled. According to the treatment pattern they received, 109 patients were placed into a control group and 82 patients into a study group (*Figure 1*).

Table 1 shows the characteristics of patients. The mean age was 42.5±12.4 years in the control group and 41.0±12.1 years in the study group, showing no significant difference (P=0.402). Most patient in both groups were male, constituting more than 75% of the total, and their mean body weight was 63.2±9.8 kg in the control group and 61.3±11.7 kg in the study group, showing no significant difference (P=0.209). About 90% of the severe burns in this study were caused by flame. While the TBSA was slightly higher in the study group than in the control group, showing no significant difference, the area of full thickness burn was much higher in the control group than in the study group (P=0.021). Inhalation injury after burn injury was seen in 42 and 39 patients in the control and study groups, respectively, and the time to resuscitation was about 5 hours in both groups. Although some patients had one or two comorbid diseases, there was no significant difference between the two groups. Baseline data of urine output and lab characteristics in both groups are shown in *Table 2*, and while the baseline level of sCr and BUN was slightly higher in the control group compared with the study group, no significant difference was found (P=0.081 and 0.089).

The resuscitation fluid volume ratio, crystalloid volume ratio, and colloid volume ratio are summarized in *Table 3*. This shows the fluid volume ratio and colloid volume ration

Table 1 Characteristics of severe burns patients

Characteristics	Control group	Study group	P value
Number	109	82	
Age (years)	42.5±12.4	41.0±12.1	0.402
Sex			0.887
Male	86 (78.9%)	64 (78.0%)	
Female	23 (21.1%)	18 (22.0%)	
Body weight (kg)	63.2±9.8	61.3±11.7	0.209
Etiology of burn injury			0.324
Flame	98 (89.9%)	77 (93.9%)	
Hot water	11 (10.1%)	5 (6.1%)	
TBSA	53.1±11.6	55.2±12.2	0.237
Area of full thickness burn	17.5±6.5	15.1±7.4	0.021
Inhalation injury	42 (38.5%)	39 (47.6%)	0.211
Time to resuscitation (hours)	5.0±2.1	5.3±2.1	0.271
Chronic comorbid diseases			
Hypertension	18 (16.5%)	14 (17.1%)	0.918
Diabetes	11 (10.1%)	10 (12.2%)	0.646
Congestive heart failure	2 (1.8%)	3 (3.7%)	0.635
Cerebrovascular accident	3 (2.8%)	3 (3.7%)	1.000
Chronic obstructive pulmonary disease	2 (1.8%)	1 (1.2%)	1.000

TBSA, total burn surface area.

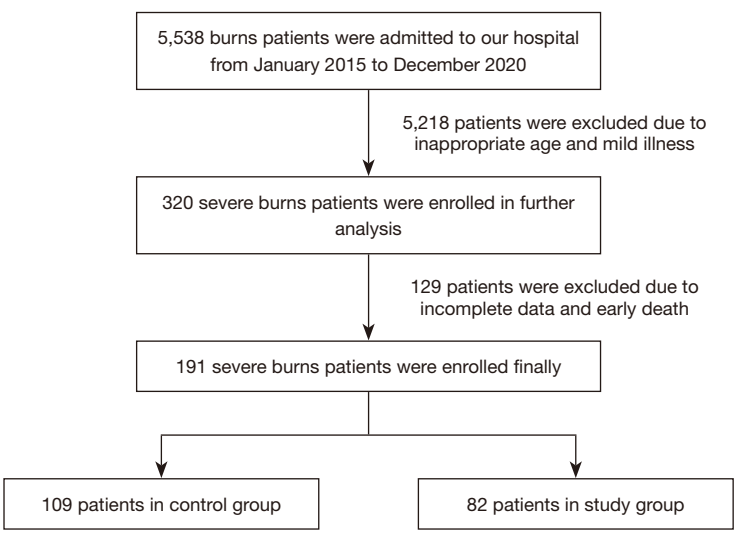

Figure 1 Flow chart.

Table 2 Baseline data of urine output and lab characteristics in severe burns patients

Characteristics	Control group	Study group	P value
Baseline urine output (mL/h)	66.3±19.4	68.0±24.6	0.613
Baseline sCr (μmol/L)	88.3±22.4	82.6±22.1	0.081
Baseline BUN (mmol/L)	7.9±1.7	7.5±1.5	0.089
Baseline CK-MB (U/L)	78.1±23.9	80.0±23.9	0.588
Baseline PCT (μg/L)	1.12±0.22	1.13±0.29	0.761

sCr, serum creatinine; BUN, blood urea nitrogen; CK-MB, creatine kinase-MB; PCT, procalcitonin.

Table 3 Resuscitation fluid volume ratio, crystalloid volume ratio and colloid volume ratio in severe burns patients

Characteristics (mL/kg/% TBSA)	Control group	Study group	P value
First 24 hours			
Resuscitation fluid volume ratio	2.59±0.39	2.29±0.40	<0.001
Crystalloid volume ratio	1.00±0.19	1.02±0.28	0.517
Colloid volume ratio	0.78±0.27	0.52±0.18	<0.001
Second 24 hours			
Resuscitation fluid volume ratio	1.90±0.44	1.73±0.39	0.007
Crystalloid volume ratio	0.76±0.18	0.72±0.24	0.147
Colloid volume ratio	0.40±0.17	0.34±0.10	0.003

TBSA, total burn surface area.

were both significantly higher in the control group than the study group in the first 24 hours (both P<0.001), and in the second 24 hours (P=0.007 and 0.003). On the other hand, there was no significant difference between the two groups in crystalloid volume ratio during the period of 48 hours.

The overall mortality of patients was relatively low with only five patients dying within 28 days and eight dying during treatment (*Table 4*). More patients had AKI and ARDS in the control group during treatment than in the study group (P=0.029 and 0.016), while about 20% patients in both groups had sepsis and 11 had venous thromboembolism (*Table 4*). The length of hospital stay in the study group was 59.3±18.3 days, which was much shorter than the 71.7±14.4 days in the control group (P<0.001), and the length of ICU stay was much shorter in the study group than in the control group (P=0.005) (*Table 4*).

Risk factors of AKI and ARDS were analyzed according to multivariable logistic regression (*Table 5*) and showed PCCO monitoring could significantly improve the incidence of AKI and ARDS in enrolled severe burns and TBSA was an important risk factor for both. In addition, the existence of inhalation injury and older age increased the incidence of ARDS after severe burns. The risk factors of length of hospital stay were then analyzed according to multivariable linear regression (*Table 6*) and identified PCCO monitoring as an important method to shorten the length of hospital stay (P=0.010). Higher TBSA and inhalation injury were related to longer hospital stay in enrolled patients, and the occurrence of burn-related complications, such as AKI, ARDS, and sepsis, prolonged the length of hospital stay.

Discussion

Although PCCO monitoring technology has been proposed for more than one decade and has been applied in clinical patients for several years, there have been no relevant studies verifying its advantages compared with conventional monitoring. Our study was the first to verify the effect of PCCO monitoring on the prognosis of severe burns patients receiving fluid resuscitation, and the results showed that it effectively reduced the incidence of burns-related

Table 4 Outcomes in severe burns patients

Characteristics	Control group	Study group	P value
Primary outcomes			
28-day mortality	3 (2.8%)	2 (2.4%)	1.000
Total mortality	4 (3.7%)	4 (4.9%)	0.727
Secondary outcomes			
AKI	32 (29.4%)	13 (15.9%)	0.029
ARDS	27 (24.8%)	9 (11.0%)	0.016
Sepsis	23 (21.1%)	16 (19.5%)	0.787
Venous thromboembolism	5 (4.6%)	6 (6.1%)	0.423
Length of hospital stay	71.7±14.4	59.3±18.3	<0.001
Length of ICU stay	59.1±13.4	53.1±15.2	0.005

AKI, acute kidney injury; ARDS, acute respiratory distress syndrome.

Table 5 Risk factors of burn-related complications in severe burns patients according to multivariable logistic regression analysis

Characteristics	Multivariable analysis	
	OR (95% CI)	P value
AKI		
PCCO monitoring	0.441 (0.192, 0.854)	0.034
TBSA	1.104 (1.067, 1.143)	<0.001
ARDS		
PCCO monitoring	0.383 (0.169, 0.871)	0.022
Older age	1.009 (1.003, 1.015)	0.034
TBSA	1.082 (1.046, 1.121)	<0.001
Inhalation injury	3.230 (1.349, 7.737)	0.009

All collected characteristics were initially analyzed using univariable logistic regression analysis and any characteristic which showing significant effects on the incidence of burns-related complications was further analyzed using multivariable logistic regression. AKI, acute kidney injury; PCCO, pulse contour cardiac output; TBSA, total burn surface area.

Table 6 Risk factors of longer length of hospital stay in severe burns patients according to multivariable linear regression analysis

Characteristics	Multivariable analysis	
	β (95% CI)	P value
PCCO monitoring	−4.333 (−7.630, −1.036)	0.010
TBSA	0.454 (0.308, 0.601)	<0.001
Inhalation injury	3.310 (0.041, 6.580)	0.047
AKI	6.997 (0.871, 13.123)	0.025
ARDS	3.183 (0.753, 5.613)	0.029
Sepsis	4.855 (1.501, 8.210)	0.016

All collected characteristics were initially analyzed using univariable linear regression analysis and any characteristic which showing significant effects on the length of hospital stay was further analyzed using multivariable linear regression. PCCO, pulse contour cardiac output; TBSA, total burn surface area; AKI, acute kidney injury; ARDS, acute respiratory distress syndrome.

complications during the treatment and shortened the length of hospital stay. This study further confirmed the superiority and reliability of PCCO monitoring compared with traditional monitoring.

Nowadays, the mortality of severe burns patients worldwide is still at a relatively high level, and has been reported as ranging between 12.2% and 47.6% (3,21,22). As our burns center has many years of experience in severe burns diagnosis and treatment, the mortality is maintained at a relatively low level, and in this study, the overall mortality of enrolled patients was 3.7% in the control group and 4.9% in the study group, respectively. The overall mortality in all enrolled patients was 4.2%, and there was no significant difference in mortality between the two groups. This relatively low mortality also made it impossible to verify the impact of PCCO monitoring on the mortality

of severe burns patients in this study. Previous studies have reported that risk factors associated with mortality included TBSA, body mass index, inhalation injury, and some serious complications (23-26). Considering the effects of PCCO monitoring on reducing burn-related complications of enrolled patients in this study, we proposed a hypothesis that it could also reduce mortality to a certain extent. However, this conclusion may need to be verified by more cases.

AKI and ARDS are the most common complications in the treatment of severe burns patients, their occurrence will significantly worsen the prognosis of patients, and our study showed that PCCO monitoring can effectively reduce their incidence. TBSA also acted as an important risk factor for AKI and ARDS. In previous studies, intra-abdominal hypertension, hypernatremia, and inhalation injury were risk factors for serious complications (27-29), while in the present study, inhalation injury was also found to be a risk factor for ARDS, but there was no significant relationship between it and AKI. Sepsis is also a common complication in severe burns patients, and we found its incidence to be 21.1% in the control group and 19.5% in the study group. Although the incidence was slightly lower in the study group, there was no significant difference between the two groups, which suggests that the occurrence of sepsis is not only related to rehydration, but also related to other risk factors. In addition, previous studies have shown that the occurrence of serious complications, such as sepsis, acute renal failure, ventilator use, and cardiac arrest, would significantly prolong the length of ICU stay and hospital stay of patients, which is consistent with the results of this study. PCCO monitoring has also been proven to shorten the length of hospital stay of patients according to multivariable linear regression.

By analyzing differences in the fluid volume index between the control group and study group, it was found that PCCO monitoring assisted liquid resuscitation could reduce the amount of liquid used, especially the amount of colloid. In the control group, excessive fluid administration may have led to the accumulation of fluid in the organs, resulting in organ edema, increased intra-abdominal pressure, and hindered pulmonary gas exchange, increasing the incidence of serious burns-related complications. This also suggests there may be excessive fluid administration in previous treatment, which needs to be corrected.

It should be noted that there were some limitations in this study. Firstly, we did not collect patient output data, which would have provided a deeper understanding of the whole treatment state and more information data of the effect of PCCO monitoring on the prognosis of severe burns patients. Secondly, the baseline data of the control group and study group were not well matched, and although multivariable logical regression and linear regression were used for adjustment, there may still be some bias in the results. Thirdly, this study was a retrospective cohort study, which inevitably carries some data deviations, and can be improved by a prospective study in the future. Fourthly, other treatments, such as infection control, nutritional support and scar repair, may also affect the prognosis of severe burn patients, which need more detailed study in the future.

Conclusions

Based on the results from this retrospective study, PCCO monitoring can be used as an effective auxiliary measure for fluid resuscitation in severely burned patients, which can effectively reduce the occurrence of some serious complications, such as AKI and ARDS, and shorten the length of hospital and ICU stay. Although the number of cases in this study is relatively small, the results provide some evidence for the use of PCCO monitoring in burns patients and can be further investigated in future studies.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://dx.doi.org/10.21037/apm-21-2587

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures

performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by institutional ethics committee of Affiliated Hospital of Jiangnan University (No. 2021011). Individual consent for this retrospective analysis was waived.

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