AN ADJUSTED IDEAL BODY WEIGHT INDEX FORMULA WITH FRESH FROZEN PLASMA (FFP) RESCUE DECREASES FLUID CREEP DURING BURN RESUSCITATION

UNE FORMULE CALCULÉE SUR LE POIDS IDÉAL ET UTILISANT LES PLASMA FRAIS CONGELÉ (PFC) RÉDUIT LE SURREMPLISSAGE

Lindsey L.,[1] Purvis M.V.,[2] Miles D.,[3] Lintner A.,[2] Scott V.,[2] McGinn K.,[4] Bright A.,[2] Kahn S.A.[5]✉

[1] School of Medicine, University of South Alabama, Mobile, AL, USA
[2] Department of Surgery, Division of Acute Care Surgery & Burns, The University of South Alabama Medical Center, Mobile, AL, USA
[3] School of Medicine, University of Mississippi, Jackson, MS, USA
[4] Department of Pharmacy Practice, Harrison School of Pharmacy, Auburn University, Mobile, AL, USA
[5] Department of Surgery, Medical University of South Carolina, Charleston, SC, USA

SUMMARY. Severe burn injury requires significant volume resuscitation, but over-resuscitation can be deadly. Accurate resuscitation of obese patients is challenging due to the decreased vascularity of adipose tissue. This study compares an adjusted ideal body weight index formula with fresh frozen plasma rescue to historical controls resuscitated with Parkland-based resuscitation. A retrospective review was conducted of adult patients admitted to our regional burn center with ≥ 20% total body surface area (TBSA) burns from 2010 to 2017 who survived more than 48 hours. Historical controls were resuscitated with Parkland-based resuscitation with occasional albumin. The adjusted ideal body weight (AIBW) patients were resuscitated with 2-4 mL/kg/%TBSA using an adjusted ideal body weight with fresh frozen plasma (FFP) rescue. Outcomes were compared with nonparametric statistics. A total of 161 patients met inclusion criteria: 40 patients received AIBW resuscitation and 121 patients were included as controls. The AIBW group received less fluid (3.30 vs. 4.15 mL/kg/%TBSA, p<0.001). A significant reduction in acute kidney injury requiring dialysis in the AIBW group was appreciated (5% vs. 19%, p=0.03) with improved mortality in AIBW patients as well (5% vs. 20%, p=0.03). Using an adjusted ideal body weight with FFP rescue to resuscitate patients with severe burn injury leads to a significant reduction in fluid administration without increase in acute kidney injury requiring dialysis and with improved mortality.

Keywords: burn, resuscitation, obesity, adjusted ideal body weight, fresh frozen plasma

RÉSUMÉ. *Les brûlés graves ont besoin d'un remplissage vasculaire majeur, pouvant toutefois être mortel s'il est exagéré. Il est particulièrement difficile chez les obèses, en raison de la faible vascularisation du tissu adipeux. Cette étude compare une formule basée sur le poids idéal (PI) et utilisant du PFC à des séries historiques utilisant la formule de Parkland. Cette étude rétrospective a revu les dossiers des patients admis dans notre CTB, ayant survécu plus de 48 h, entre 2010 et 2017. Les 121 cas historiques recevaient un remplissage selon Parkland (et de l'albumine au besoin). Les 40 patients à l'étude recevaient 2 à 4 mL/kg/% de PFC, le volume étant calculé sur le poids idéal. Ce groupe recevait significativement (p < 0,001) moins (3,3 mL/kg/%) de volume que le groupe contrôle (4,15). Ils avaient aussi moins fréquemment besoin d'épuration extra- rénale (5% VS 19%, p= 0,03) et leur mortalité était moindre (5% VS 20%, p= 0,03).*

Mots-clés: *brûlure, remplissage vasculaire, obésité, poids idéal, plasma frais congelé*

✉ Corresponding author: Dr. Steven Kahn, Department of Surgery, Division of Acute Care Surgery, Medical University of South Carolina, 96 Jonathan Lucas St, Charleston, SC, USA. Tel.: +1 8437923780; email: kahnst@musc.edu
Manuscript: submitted 16/03/2020, accepted 24/04/2020

Introduction

The ideal formula and fluid for resuscitation remains a clinical controversy in acute burn treatment. It is well established that fluid resuscitation needs to be optimized during the first 24 to 48 hours to maintain tissue perfusion and prevent shock in burn patients.[1,2] However, the proper fluid composition and volume of resuscitation is still controversial. Initial attempts at finding optimal fluid formulations led to investigations that began with crystalloid, then transitioned to whole blood, blood components, and later purified albumin.[3-5] However, by the early 1970s, most centers abandoned this practice in favour of crystalloid solutions, given the lack of ability to safely use blood products.[6] Today, crystalloid-based resuscitation remains the most common practice at the majority of burn centers.[6,7]

The current Advanced Burn Life Support (ABLS) guidelines for adult patients recommend fluid resuscitation of 2-4 mL/kg body weight x % total body surface area burn per hour of lactated ringer's (LR) to maintain a minimum hourly urine output (UOP) of 0.5 mL/kg/hour.[8] A recent survey validated that the majority of burn centers follow the ABLS guidelines to resuscitate burn patients.[7] However, using these guidelines, a shift from under resuscitation of patients to over resuscitation has been observed.[8,9] This trend toward over resuscitation was first noticed and illustrated in 2000 as a "swing in the resuscitation pendulum".[8]

Numerous studies have demonstrated that burn patients receive more crystalloid fluids than what is currently recommended in the ABLS guidelines.[10-18] This paradox is often referred to as "fluid creep," which was first coined by Pruitt et al. in the year 2000.[9-11] Later, the "supra-Baxter phenomenon" showed that burn patients treated in the year 2000 were noted to have received over twice the volume of crystalloid compared to matched patients in 1970.[16] Thus, the amount of fluid that patients receive has increased over time.

While under resuscitation may lead to organ hypoperfusion, over resuscitation is not without risk. High volume resuscitation may lead to multiple complications including pulmonary edema, respiratory failure, prolonged mechanical ventilation, acute kidney injury, conversion of partial thickness burns, and compartment syndrome of the extremities and abdomen.[19-25] Ultimately, these complications of over resuscitation may lead to preventable procedures and increase the risk of death in critically ill burn patients.[19]

The intricacies of burn resuscitation become increasingly difficult when applied to the obese population. Obese patients are particularly challenging to resuscitate due to the decreased vascularity of adipose tissue and risk of over resuscitation utilizing a formula based on actual body weight. Unfortunately, there is a paucity of high-quality literature on how best to resuscitate the obese burn patient. Several retrospective studies have demonstrated that obese burn patients have increased hospital length of stay (LOS) and higher rates of mortality compared to patients with a normal body mass index (BMI).[26,27] Additionally, obese patients typically require less fluid per kg of actual body weight to achieve resuscitation goals.[28] In 2017, Liu et al. demonstrated that with increasing percent difference from ideal body weight patients required lower fluid volumes for resuscitation and had a correlation with increased risk for mortality.[26] Therefore, in obese patients, the use of actual body weight to calculate fluid resuscitation requirements likely often leads to over resuscitation.

The utilization of colloid fluids may also play an important role in burn resuscitation. Given the oncotic characteristics, colloids may naturally preserve intravascular volume compared to crystalloids and, theoretically, reduce fluid resuscitation requirements. Most burn centers use some type of colloid as rescue therapy in the resuscitation of burn patients, usually employing either albumin or fresh frozen plasma (FFP).[7] Historically, albumin has been used frequently in clinical practice, however, in the 1990s, there was a resurgence of FFP utilization in burn patients.[29,30] Subsequently, recent studies have demonstrated that burn patients who were transfused plasma received less fluid volume overall than those who did not.[29,30]

The benefits of FFP may not only be due to its colloidal properties. Under normal circumstances, the glycoprotein-polysaccharide matrix, or glycocalyx, functions as a barrier to decrease vascular permeability, inhibit coagulation, and reduce leukocyte

adhesion in blood vessels.[31-33] In shock states, disruption in syndecan-1 may lead to glycocalyx degradation and endothelial damage.[34,35] In recent in vivo and in vitro studies, FFP has been shown to protect the syndecan backbone of the glycocalyx. Therefore, FFP may decrease endothelial cell permeability compared to crystalloid fluids and correct trauma induced coagulopathy.[34] A recent prospective, randomized trial of burn patients concluded that patients resuscitated with plasma received less crystalloid volume and had a lower incidence of intra-abdominal hypertension compared to those who did not receive FFP.[36] Recent discoveries regarding the pathophysiology of capillary leak and the role of plasma to restore the glycocalyx may offer an explanation for improved outcomes in burn patients resuscitated with plasma.

The purpose of this study was to compare the utilization of an adjusted ideal body weight (AIBW) index formula with FFP rescue to historical controls resuscitated with Parkland-based resuscitation and albumin. Adjusted body weight calculations were initially developed for the obese patient population in the critical care and dialysis setting for the increased distribution pattern seen with hydrophilic medications.[37] We hypothesized that utilization of the AIBW index formula and FFP would lead to decreased volumes of resuscitation in critically ill burn patients and improve patient outcomes compared to historical controls. As most patients will have low-vascularity adipose tissue that does not require resuscitation, this formula would be applicable to all patients regardless of obesity status.

Materials and methods

Study design

A retrospective review of patients admitted to a regional burn center between January 2010 and September 2017 was performed. The study methods and design were reviewed and approved by the Institutional Review Board prior to data collection. Critically ill burn patients presenting within 24 hours of injury with greater than or equal to 20% total body surface area (TBSA) burn were included. Patients less than 17 or greater than 79 years of age and those who did not survive to 48 hours or who were put on comfort care within the first four days were excluded. Patients were stratified into two groups: a "historical control" group and an "adjusted ideal body weight index" (AIBW) group.

Historical controls between January 2010 and May 2014 were resuscitated with the Parkland formula utilizing crystalloid fluids and albumin. Any fluids administered prior to arrival at the emergency department were added to the 24-hour total. Albumin rescue was administered at the discretion of the providing physician for oliguria.

Patients in the protocol group were resuscitated between June 2014 and September 2017 using an AIBW index (AIBW = ideal body weight + 0.3 [actual body weight – ideal body weight]). Fluid resuscitation targets were calculated as 2-4 mL/AIBW in kg/%TBSA. The initial fluid rate was calculated using degree of burn and presence or absence of inhalation injury. Patients with second degree burns without inhalation injury received 2 mL/AIBW/%TBSA. Patients with second degree burns and inhalation injury or third degree burns received 3 mL/AIBW/%TBSA. Patients with third degree burns and inhalation injury received 4 mL/AIBW/%TBSA. Fluids were titrated 10-20% per hour based on a deviation from target UOP of 0.5 mL/AIBW/hour using the algorithm displayed in *Fig. 1*. If oliguric for more than two hours despite

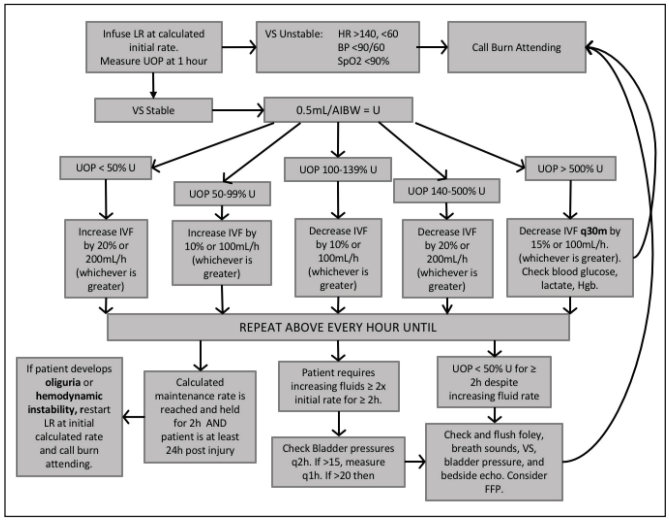

Fig. 1 - AIBW resuscitation algorithm
LR = lactated ringers; UOP = urine output; VS = vital signs; HR = heart rate; BP = blood pressure; SpO2 = peripheral capillary oxygen saturation; AIBW= adjusted ideal body weight; U = 0.5mL/AIBW; IVF = intravenous fluids; mL/h = milliliters/hour; m = minute; Hgb = hemoglobin; Echo = echocardiogram; FFP = fresh frozen plasma

crystalloid administration, patients were assessed for etiology with exam and often an ultrasound of the inferior vena cava. If hypovolemic, 1-2 units of FFP were administered as rescue therapy.

Demographic and injury data collected for each patient included age, gender, weight, degree of burn, and presence of inhalation injury by direct bronchoscopy (in the AIBW group). In the historical control group, inhalation injury was a clinical diagnosis made by the burn team and often was not confirmed by bronchoscopy. In the AIBW group, bronchoscopy was used to diagnose inhalation injury. Other data collected included the volume and type of fluids administered in the first 24 hours post injury, as well as UOP (in mL/kg/hour) for the first 24 hours. Patient outcomes collected included need for escharotomy, acute kidney injury (AKI) requiring dialysis, need for tracheostomy, inpatient mortality, ventilator free days at day 30, and intensive care unit (ICU) and hospital length of stay (LOS).

Statistical analysis

Analysis was performed using the R Language, a well-known open source statistical software package.[38] Nonparametric data were analyzed using Fisher's Exact test, and Mann-Whitney U test was used for continuous variables. Data are presented as median [interquartile range] unless otherwise noted. A p value of <0.05 was considered significant for all analyses.

Results

Demographics and injury data

Over the 7-year, 8-month period, 156 patients with greater than or equal to 20% TBSA burns qualified for inclusion. Forty patients were resuscitated with the AIBW protocol, while 116 patients represented the historical control group. Demographics and injury characteristics were comparable for the two groups (*Table I*). There were no significant differences in age, gender, weight or burn size between the AIBW and control groups. The median age was 44.5 [32,58] years for the AIBW group and 37.5 [30.9,52.6] years for the control group (p=0.27). Gender was 87% male in the AIBW group and 80% male in the control group (p=0.35). There was no significant difference in median total body weight in the AIBW group: 88.25 kg [74.5,104] compared to the control group 84 kg [72,97.5], (p=0.49). Burn size was comparable between groups: 33.8% TBSA in the AIBW group vs. 31% TBSA in the control group (p=0.9). However, 53% (n=61) of control group patients had a diagnosis of inhalation injury compared to 25% of AIBW patients (n=10), (p=0.003).

Table I - Patient demographics and injury data

Characteristic	Control Group (n = 116)	AIBW Group (n = 40)	P
Age (years)	37.5 [30.9,52.6]	44.5 [32,58]	0.27
Gender Male, % Female, %	 80 (n=93) 20 (n=23)	 87 (n=35) 12 (n=5)	0.35
Weight (kg)	84.0 [72,97.5]	88.3 [74.5,104]	0.49
% TBSA burn	31.0 [24,46.8]	33.8 [22,54]	0.9
Inhalation injury, %	53 (n=61)	25 (n=10)	0.003

Outcomes are reported as median [interquartile range] unless otherwise noted; kg = kilograms; TBSA = total body surface area; AIBW = adjusted ideal body weight

Outcomes

The AIBW group received significantly less fluid volume in the first 24 hours compared to the control group: 3.16 [2.1,4.3] mL/kg/% TBSA versus 4.16 [3.1,5.7] mL/kg/%TBSA (p=0.0001, *Table II*). UOP

Table II - Results

Outcome	Control Group (n= 116)	AIBW Group (n = 40)	P
Fluid administered in first 24 hours (mL/kg/hr)	4.16 [3.1,5.7]	3.16 [2.1,4.3]	0.0001
UOP in first 24 hours (mL/kg/hr)	1.45 [0.9,2.1]	1.01 [0.6,1.3]	<0.0001
AKI requiring dialysis, %	20 (n=23)	5 (n=2)	0.03
ICU length of stay (days)	14 [8,30.75]	27.5 [12.75,41]	0.02
Hospital length of stay (days)	17.5 [11,37.5]	28.5 [21,51]	0.004
Mortality, %	20 (n=23)	5 (n=2)	0.03
Ventilator-free days of 30	23.0 [17,30]	27 [24,30]	0.14
Tracheostomy, %	19 (n=22)	13 (n=5)	0.47
Escharotomy, %	17 (n=20)	25 (n=10)	0.35

Outcomes are reported as median [IQR] unless otherwise noted; UOP = urine output; AKI = acute kidney injury; ICU = intensive care unit; Ventilator-free days calculated as number of days during the first thirty days of admission in which the patient did not require mechanical ventilation

in the first 24 hours was also decreased in the AIBW group: 1.01 [0.6,1.3] mL/kg/hour versus 1.45 [0.9,2.1] mL/kg/hour (p<0.0001). Despite the decrease in UOP, there was a significant decrease in AKI requiring dialysis during hospital admission in the AIBW group compared to historical controls: 5% (n=2) versus 20% (n=23), (p=0.03). The use of the AIBW algorithm was also associated with a significant reduction in mortality from 20% (n=23) in the control group to 5% (n=2) in the AIBW group (p=0.03). However, there was no difference in ventilator-free days at day 30 between groups: 27 [24,30] days in the AIBW group versus 23 [17,30] days in the control group (p=0.14). The AIBW group had a longer hospital LOS of 28.5 [21,51] days compared to 17.5 [11,37.75] days in the control group (p=0.004), as well as a longer ICU LOS of 27.5 [12.75,41] days versus 14 [8,30.75] days (p=0.02). No differences in escharotomy 25% (n=10) in the AIBW group versus 17% (n=20) in the control group (p=0.35) or tracheostomy 13% (n=5) in the AIBW group versus 19% (n=22) in the control group (p=0.47) were noted.

Discussion

The burn resuscitation conundrum remains a challenge to even the most experienced providers. The goal is to find a balance between maintaining organ perfusion, while still minimizing the amount of volume administered. Retrospective and prospective studies comparing fluid volumes, colloid versus crystalloid, and type of colloid have begun to clarify the resuscitation process. The aim of this retrospective study was to compare the utilization of an adjusted ideal body weight index formula with FFP rescue to historical controls resuscitated with high volume, Parkland-based formulas. By using an adjusted formula titrated by ideal weight, fluid resuscitation parameters are universally applicable. Those in the obese category receive the adjusted amount, while patients with normal or underweight BMI autocorrect to the appropriate fluid amount for their actual body weight. The findings of this study confirm that using an adjusted ideal body weight formula decreased the total amount of resuscitation fluid administered while improving the morbidity and mortality in patients. Of the 40 patients resuscitated with the AIBW formula as compared to historical controls, a decreased resuscitative fluid requirement of 1 mL/kg/hr was noted. In addition, patients in the treatment group had a decreased UOP of approximately 0.44 mL/kg/hr with a corresponding decrease in the incidence of AKI requiring dialysis. There was an increase in hospital and ICU length of stay in the treatment group; however, these differences are likely due to the fact that a higher percentage of patients survived, meaning more time in the hospital. In addition, during the time of the AIBW group, the burn center was utilizing more early comfort care and hospice for non-survivable injuries. In contrast, the historical group had multiple patients with non-survivable injuries that were resuscitated and survived several days to 2 weeks. In addition, patients with more comorbidities tend to survive longer with advances in critical care. Many patients with comorbid conditions that were deemed non-survivable when coupled with severe burn injury as little as 10 years ago now survive. In addition, obesity and substance dependence are now more frequently seen across the United States, not limited to the burn population, further confounding a study using historical controls. Regardless, overall mortality decreased from 20% to 5% in patients resuscitated with the AIBW formula. The authors only partially attribute this to the resuscitation formula and subsequent decreased fluid administration, but suspect unmeasured confounders in other aspects of care advancement over time play a role as well. In particular, wound care strategies, surgical approaches, general advancements in critical care, and other difficult-to-measure factors likely played a role in the mortality statistics.

Recently, much has been published regarding AKI in burn injury.[39-42] AKI in burn patients, even those with smaller TBSA burns, is unfortunately very common.[42] AKI is associated with increased morbidity and mortality up to years after the initial injury.[40,42] Although this study evaluated the incidence of AKI requiring dialysis, the study does not quantify incidence stage or duration of AKI. As Xue et al. have recently noted, these factors are important to evaluating AKI after burn injury.[41] However, de-

creasing the incidence of AKI requiring dialysis with the use of the AIBW protocol profoundly impacts burn patient morbidity and mortality.

A key element of the resuscitation protocol lies in the calculation of fluid requirement by burn depth and presence of inhalation injury. Faraklas et al. showed that patients with deeper burns, larger TBSA, and inhalation injury more often develop capillary leak which necessitates greater volumes of resuscitative fluids, including colloid resuscitation.[43] This theory bolsters the notion that resuscitation should be individualized and was the basis for the resuscitation protocol implemented in the treatment group. The standard 4 mL/kg/hr of crystalloid denoted by the Parkland formula does not account for burn depth or the presence of inhalation injury and likely contributes to over resuscitation.[28,44,45] By initiating fluid administration based on depth of burn and presence of inhalation injury, the AIBW protocol creates a reasonable set point by which resuscitation may be titrated to meet UOP goals while still preventing the pendulum swing to fluid creep.

Multiple studies have shown that colloid rescue can reduce fluid requirements in burn injury by decreasing capillary leak.[19,35,45] The recent theories of colloid restoration of the glycocalyx barrier in the endothelium reinforces these thoughts.[28,32,34,46-47] However, the colloid versus crystalloid debate continues among burn providers.[43] Few prospective studies exist that assess fluid type, and those that have been conducted are often poorly powered and performed at a single center. Currently, individual burn surgeons ultimately decide when to begin colloids and what type to use.[7] Based on the outcomes of this study, early and judicious use of FFP may decrease overall burn fluid requirement and, therefore, reduce over resuscitation morbidity and mortality.

While the outcomes of this study are impactful to clinical practice, there are some limitations to the study. First, it is a retrospective review at a single center. Additionally, there were patients in both groups who did not require colloid. They often had less severe burns and lower incidence of inhalation injury, making extrapolation of the role of the type of colloid more difficult. Furthermore, the occurrence of inhalation injury was significantly less in our AIBW group as compared to the historic control group, which may have affected the volume of fluid necessary for resuscitation. The lower frequency of inhalation injury is likely attributed to a more stringent protocol of diagnosis of inhalation injury with direct bronchoscopy that was implemented in the latter half of the study for the control group. When reviewing the medical records of the historical control patients, it was noted that many of the patients carried a diagnosis of inhalation injury but did not follow the clinical course of a patient with such, based on ventilator days and other respiratory parameters. The control group likely had many false positives, and the 53% rate of inhalation injury is essentially twice as high as expected when one looks at national data, which is more in line with what was found in the AIBW group. However, the burn size was equivalent, indicating that the severity of burn injury was comparable between the two groups. The patient weights were also equivalent as well, suggesting that variations in size probably did not play a role in the difference in outcomes. Future, prospective studies that include a larger patient population are needed to validate the outcomes of this study and increase the power of the results. In addition, a more in-depth analysis comparing BMI in obese patients would be helpful. Fortunately, this formula autocorrects based on BMI, as patients with a normal weight receive fluid at a rate based on their ideal body weight (or very close to it). The more obese someone is, the greater the reduction in the weight-based resuscitation.

Looking forward, the authors are working to further elucidate the impacts of AIBW index specifically in the obese population as compared to patients with normal BMI. In addition, the resuscitation formula has been simplified since the analysis presented in this manuscript was completed. Still using AIBW, fluid resuscitation now begins with 2cc/kg/%TBSA for almost all comers. Only the patients with a high grade (AIS 3 or 4) and all full thickness injury are initially resuscitated with 3cc/kg/%TBSA. Empiric results over a 1-year period are encouraging, with no patient requiring dialysis. Additionally, measuring markers of endothelial integrity will also be necessary to determine the role of FFP in attenuating capillary leak and thereby limiting the amount of crystalloid resuscitation. Finding

a balance between maintaining adequate organ perfusion and preventing over resuscitation exists by eliminating the resuscitation of extraneous adipose tissue, titrating initial fluids by injury severity, and using FFP to decrease capillary leak.

When one presents the concept of reducing the amount of fluid during burn resuscitation, the logical follow up question is "Will it lead to more complications related to hypovolemia?" When one looks at the data presented about the AIBW in isolation, it shows that the answer is "No - the formula is safe." Patients received less fluid than would have been predicted with traditional Parkland formula (3.16 instead of 4cc/kg/%TBSA), had a favourable rate of AKI requiring dialysis, and had better than expected mortality in such a cohort of critically ill burn patients. A mortality rate of 3% for an entire cohort of inpatients treated at a burn center is widely regarded to be standard and acceptable. This group of >20% TBSA burn patients had a mortality rate of 3%. Some of the limitations and confounders above limit the conclusions one can draw from this manuscript regarding which fluid strategy is definitively better. However, the data presented regarding the AIBW group demonstrates that it is certainly a safe formula and is associated with less fluid administration.

Conclusion

The AIBW formula with FFP rescue appears to be a safe and effective method of burn resuscitation. The AIBW patients received less fluid than traditional Parkland formula-resuscitated control patients without an increase in AKI requiring dialysis, although there were some limitations to the data set. The use of the AIBW formula was also associated with a reduction in mortality. Optimization, individualization, and protocolization of fluid resuscitation is key to preventing the many grave complications associated with over resuscitation.

BIBLIOGRAPHY

1 Pham TN, Cancio LC, Gibran NS: American Burn Association Practice Guidelines Burn Shock Resuscitation. J Burn Care Rehabil, 29(1): 257-266, 2008.
2 Cancio LC, Salinas J, Kramer GC: Protocolized resuscitation of burn patients. Crit Care Clin, 32(4): 599-610, 2016.
3 Cope O, Moore FD: The redistribution of body water and the fluid therapy of the burned patient. Ann Surg, 126: 1010-45, 1947.
4 Evans EI, Purnell OJ, Robinett PW, Batchelor A et al.: Fluid and electrolyte requirements in severe burns. Ann Surg, 135: 804-17, 1952.
5 Janeway CA, Gibson ST, Woodruff LM, Heyl JT et al.: Chemical, clinical, and immunological studies on the products of human plasma fractionation. VII. Concentrated human serum albumin. J Clin Invest, 23: 465-90, 1944.
6 Greenhalgh DG: Burn resuscitation. J Burn Care Res, 28: 555-65, 2007.
7 Greenhalgh DG: Burn resuscitation: the results of the ISBI/ABA survey. Burns, 36: 176-82, 2010.
8 ABLS Guidelines, 2007: 1-114.
9 Pruitt BA, Jr: Protection from excessive resuscitation: "pushing the pendulum back". J Trauma, 49: 567-8, 2000.
10 Cartotto R, Zhou A: Fluid creep: the pendulum hasn't swung back yet! J Burn Care Res, 31: 551-8, 2010.
11 Saffle JR: The phenomenon of "fluid creep" in acute burn resuscitation. J Burn Care Res, 28(3): 382-395, 2007.
12 Blumetti J, Hunt JL, Arnoldo BD, Parks JK et al.: The Parkland formula under fire: is the criticism justified? J Burn Care Res, 29: 180-6, 2008.
13 Cancio LC, Chávez S, Alvarado-Ortega M et al.: Predicting increased fluid requirements during the resuscitation of thermally injured patients. J Trauma, 56: 404-14, 2004.
14 Cartotto RC, Innes M, Musgrave MA, Gomez M, Cooper AB: How well does the Parkland formula estimate actual fluid resuscitation volumes? J Burn Care Rehabil, 23: 258-65, 2002.
15 Engrav LH, Colescott PL, Kemalyan N et al.: A biopsy of the use of the Baxter formula to resuscitate burns or do we do it like Charlie did it? J Burn Care Rehabil, 21: 91-5, 2000.
16 Friedrich JB, Sullivan SR, Engrav LH et al.: Is supra-Baxter resuscitation in burn patients a new phenomenon? Burns, 30: 464-6, 2004.
17 Ivy ME, Atweh NA, Palmer J, Possenti PP et al.: Intra-abdominal hypertension and abdominal compartment syndrome in burn patients. J Trauma, 49: 387-91, 2000.
18 Mitra B, Fitzgerald M, Cameron P, Cleland H: Fluid resuscitation in major burns. ANZ J Surg, 76: 35-8, 2006.
19 Salisbury R: Increased fluid resuscitation can lead to adverse outcomes in major-burn injured patients, but low mortality is achievable. Yearbook of Plastic and Aesthetic Surgery, 2010: 95-96, 2010.
20 Klein MB, Hayden D, Elson C et al.: The association between fluid administration and outcome following major burn: a multicenter study. Ann Surg, 245: 622-8, 2007.
21 Greenhalgh DG, Warden GD: The importance of intra-abdominal

pressure measurements in burned children. J Trauma, 36: 685-90, 1994.
22 Ivy ME, Possenti PP, Kepros J et al.: Abdominal compartment syndrome in patients with burns. J Burn Care Rehabil, 20: 351-3, 1999.
23 Oda J, Yamashita K, Inoue T et al.: Resuscitation fluid volume and abdominal compartment syndrome in patients with major burns. Burns, 32: 151-4, 2006.
24 Strang SG, Van Lieshout EM, Breederveld RS, Van Waes OJ: A systematic review on intra-abdominal pressure in severely burned patients. Burn, 40: 9-16, 2014.
25 Markell KW, Renz EM, White CE et al.: Abdominal complications after severe burns. J Am Coll Surg, 208: 940-7; discussion 947-9, 2009.
26 Liu NT, Fenrich CA, Serio-Melvin ML, Peterson WC et al.: The impact of patient weight on burn resuscitation. J Trauma Acute Care Surg, 83: S112-S119, 2017.
27 Rae L, Pham TN, Carrougher G et al.: Differences in resuscitation in morbidly obese burn patients may contribute to high mortality. J Burn Care Res, 34(5): 507-514, 2013.
28 Benicke M, Perbix W, Lefering R et al.: New multifactorial burn resuscitation formula offers superior predictive reliability in comparison to established algorithms. Burns, 35(1): 30-35, 2009.
29 Du G, Slater H, Goldfarb IW: Influences of different resuscitation regimens on acute early weight gain in extensively burned patients. Burns, 17: 147-50, 1991.
30 Aharoni A, Abramovici D, Weinberger M et al.: Burn resuscitation with a low-volume plasma regimen-analysis of mortality. Burns, 15: 230-232, 1989.
31 Pries AR, Secomb TW, Gaehtgens P: The endothelial surface layer. Pflugers Arch, 440: 653-666, 2000.
32 Nieuwdorp M, Meuwese MC, Vink H et al.: The endothelial glycocalyx: a potential barrier between health and vascular disease. Curr Opin Lipidol, 16: 507-511, 2005.
33 Cines DB, Pollak ES, Buck CA et al.: Endothelial cells in physiology and in the pathophysiology of vascular disorders. Blood, 91: 3527-3561, 1998.
34 Kozar RA, Peng Z, Zhang R et al.: Plasma restoration of endothelial glycocalyx in a rodent model of hemorrhagic shock. Anesthesia & Analgesia, 112(6): 1289-1295, 2011.
35 Rehm M, Bruegger D, Christ F et al.: Shedding of the endothelial glycocalyx in patients undergoing major vascular surgery with global and regional ischemia. Circulation, 116: 1896-1906, 2007.
36 Latenser B: A prospective, randomized evaluation of intra-abdominal pressures with crystalloid and colloid resuscitation in burn patients. Yearbook of Critical Care Medicine, 2006: 109-110, 2006.
37 Bouguegneau A, Vidal-Petiot E, Moranne O et al.: Creatinine-based equations for the adjustment of drug dosage in an obese population. Br J Clin Pharmacol, 81: 349-361, 2016.
38 R Core Team: R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria, 2017. https://www.R-project.org/
39 Kimmel LA, Wilson S, Walker RG et al.: Acute kidney injury: it's not just the 'big' burns. Injury, 49(2): 213-218, 2017.
40 Thalji SZ, Kothari AN, Kuo PC, Mosier MJ: Acute kidney injury in burn patients: clinically significant over the initial hospitalization and 1 year after injury: an original retrospective cohort Study. Ann Surg, 266(2): 376-82, 2017.
41 Xue FS, Liu YY, Yang GZ: Assessing clinical significance of acute kidney injury in burn patients. Ann Surg, 268(6): 55-61, 2018.
42 Clark A, Neyra JA, Madni T et al.: Acute kidney injury after burn. Burns, 43(5): 898-908, 2017.
43 Faraklas I, Cochran A, Saffle J: Review of a fluid resuscitation protocol. J Burn Care Res, 33(1): 74-83, 2012.
44 Latenser B: Another important factor affecting fluid requirement after severe burn: a retrospective study of 166 burn patients in Shanghai. Yearbook of Critical Care Medicine, 2012: 55-56, 2012.
45 Goodwin CW, Dorethy J, Lam V, Pruitt BA: Randomized trial of efficacy of crystalloid and colloid resuscitation on hemodynamic response and lung water following thermal injury. Ann Surg, 197(5): 520-531, 1983.
46 Peng Z, Pati S, Potter D et al.: Fresh frozen plasma lessens pulmonary endothelial inflammation and hyperpermeability after hemorrhagic shock and is associated with loss of syndecan 1. Shock, 40(3): 195-202, 2013.
47 Johansson PCAI, Henriksen HH, Stensballe J et al.: Traumatic endotheliopathy: a prospective observational study of 424 severely injured patients. Ann Surg, 265(3): 597-603, 2017.