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RESEARCH

Rizal D. Aportadera formula versus Parkland formula in the fluid resuscitation of patients with burn injuries: cohort study

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ABSTRACT

Background. Fluid management is crucial during the first 24 hours after a burn injury due to different systemic responses of the body.
Objective. To compare the outcomes of patients with partial- or full-thickness burns initially managed using the Parkland (PRK) formula with those initially managed using the Rizal D. Aportadera (RDA) formula, a fluid resuscitation formula with added sodium bicarbonate.
Design. Cohort study.
Setting. RDA Burn Unit of Southern Philippines Medical Center, Davao City, from January 2008 to December 2018.
Participants. 181 male and female patients, aged 7 months to 78 years, with partial- or full-thickness burns.
Main outcome measures. Proportions of patients with prolonged hospital stay, sepsis, and death; odds ratio of having the outcomes for selected factors.
Main results. Of the 126 males and 55 females, with overall mean age 25.70 ± 20.92 years, included in this study, 175 (96.69%) had partial-thickness burns and 6 (3.31%) had full-thickness burns. Among the patients, 108/181; 59.67% were managed with the PRK formula, while 73/181 (40.33%) were managed with the RDA formula during fluid resuscitation. Compared to the PRK group, the RDA group had significantly lower mean length of hospital stay (11.67 ± 9.69 days vs 17.22 ± 20.45 days; p=0.0317) and lower proportion of patients with prolonged hospital stay (2/73, 2.74% vs 13/108, 12.04%; p=0.0287). Full-thickness burns had independent association with prolonged hospital stay, while major burns had independent association with death.
Conclusion. Compared to patients in the PRK group, those in the RDA group had significantly shorter hospital stay. Full-thickness burns and major burns were independently associated with prolonged hospital stay and death, respectively.

Keywords. sodium bicarbonate, Ringer's lactate, prolonged hospital stay, total body surface area, sepsis

INTRODUCTION

Fluid management is a critical step in burn treatment because of the severe fluid loss that ensues after a burn injury.[1 2] Severe burn causes the body to release different inflammatory and vasoactive mediators, usually within 24 hours after the injury. Together with other systemic responses, e.g., metabolic response such as acidosis,[3 4] these mediators can cause hypovolemia and hypoperfusion.[5]

The Parkland (PRK) formula is the most well-known and widely used protocol used to calculate fluid resuscitation in patients with severe burn injuries.[6] This formula is generally used for patients with large second-degree (deep partial-thickness) or third degree (full-thickness) burns of more than 20% of the total body surface area (TBSA) in adults, and more than 10% TBSA in children and the elderly.[7] The PRK formula uses 4 ml of Ringer's lactate solution per kilogram body weight in adults (3 ml/kg body weight in children) for every percent TBSA with partial and/or full-thickness burn injuries, with one-half of the total fluids given during the first eight hours after injury, and the second half during the next 16 hours.[8-11] Aggressive fluid resuscitation of patients within the first 24 hours of burn injury prevents worsening of hypovolemic

IN ESSENCE

Fluid resuscitation is very important in burn management due to the severe fluid loss after a burn injury.

In this cohort study among patients with partial- or full-thickness burns, those who received sodium bicarbonate in addition to Ringer's lactate during fluid resuscitation phase had shorter hospital stay compared to those who were managed using Ringer's lactate alone.

Full-thickness burns and major burns were independently associated with prolonged hospital stay and death, respectively.

shock and further acidosis.[5] Although the PRK formula is a time-tested and valuable approach in the initial fluid resuscitation of acute burns, its adequacy has been questioned in recent studies due to its underestimation of fluid resuscitation volumes, especially in patients with inhalation injury,[9] or its overestimation of fluid requirements in the first 24 hours of burn injury.[6]

Since the opening of the Rizal D. Aportadera (RDA) Burn Unit, formerly Mindanao Burn Unit, in Southern Philippines Medical Center (SPMC) in 1989, surgery residents, nurses, and other members of the Burn Team have been following a protocol to guide them in the management and care of patients with burn injuries. This management protocol, designed by Dr. Aportadera, uses a fluid resuscitation approach that incorporates the use of sodium bicarbonate. The addition of sodium bicarbonate transports an adequate amount of sodium to restore transmembrane potential and prevent cell death,[12] and transfers extracellular potassium into the cells, thereby addressing the problem of hyponatremia and hyperkalemia, respectively, in the first phase of burn injury.[1] The RDA formula uses one liter of Ringer's lactate and an additional 100 milliequivalents (mEq) of sodium bicarbonate in adults (50 mEq in children) in the fluid resuscitation approach. For both adults and children, the total 24-hour resuscitation amount is 2 ml/kg body weight per percent of TBSA with partial and/or full-thickness burn injuries. As with the PRK formula, half of the total amount is administered during the first eight hours of resuscitation, and the rest is given within the succeeding 16 hours. While this formula has been widely used in SPMC for the last 30 years, a formal recommendation for its adoption in burn management protocols has yet to be made.

We did this study to compare the outcomes of patients with partial- or full-thickness burns initially managed using the PRK formula with those among patients initially managed using the RDA formula.

METHODOLOGY

Setting

We did a retrospective cohort study among patients previously admitted at the RDA Burn Unit of SPMC. This burn unit, established in 1989, admits an average of 60 patients annually.

Participants

All patients with partial- or full-thickness burns admitted within 24 hours from the burn incident from January 2008 to December 2018 and who needed acute care and fluid resuscitation were eligible for inclusion in the study. For the purposes of this study, patients classified as having partial-thickness burns include those with either or both superficial partial-thickness and deep partial-thickness burn injuries, while patients classified as having full-thickness burns include those with full-thickness burn injuries only, as well as those with both full-thickness plus some partial-thickness burn injuries. We excluded patients who were resuscitated from other institutions and eventually transferred to SPMC. We estimated the sample size for this study using StatCalc from Epi Info™ 7.2.2.6 based on the assumptions that 66.67% of patients with >20% TBSA burns managed using the PRK formula die,[13] that the ratio of patients managed with PRK formula and RDA formula is 1.5, and that death among patients managed using the RDA formula is 21% lower than those managed using the PRK formula. In a computation for odds ratio to determine the association of selected clinical factors with death, carried out with <5% level of significance, a total sample size of at least 180 patients will have 80% power of rejecting the null hypothesis—no significant increase or decrease in odds ratio—if the alternative holds.

Data collection

We reviewed the medical records of each patient included in the study. From the records, we collected data on age, sex, type of burn, burn severity, TBSA affected by the burn, and comorbidities [hypertension, diabetes mellitus (DM), others]. We also collected the recorded the blood pressure (BP), heart rate, Glasgow Coma Scale score (GCS)/Alert-Voice-Pain-Unresponsive (AVPU) scale, urine output, arterial blood gases (ABG), white blood cell count (WBC), serum sodium, serum potassium, and serum creatinine upon admission. From the records, we classified patients as having been managed using the RDA formula (RDA group) if sodium bicarbonate was used in the fluid management. Otherwise, we classified the patient as having been managed using the PRK formula (PRK group).

We categorized admitting vital signs and laboratory results using the following cut-offs: hypotension—systolic blood pressure (SBP) <90mmHg or diastolic blood pressure (DBP) <60mmHg for patients aged 16 years and above,[14] or hypotension according to the pediatric blood pressure chart from Children's Health Center[15] for patients below 16 years old; hypertension—SBP ≥140mmHg or DBP of ≥90mmHg for patients aged 16 years and above,[16] or hypertension according to the pediatric blood pressure chart from Children's Health Center[15] for patients below 16 years old; bradycardia—heart rate <50 beats per minute (bpm); tachycardia—heart rate >110 bpm for adult patients, or tachycardia according to the pediatric vital signs by Fowler[17] for patients below 18 years old; leukopenia—WBC <5x10^3/uL; leukocytosis—WBC >10 x10^3/uL; hyponatremia—serum sodium <136 mmol/L; hypernatremia—serum sodium >144 mmol/L; hypokalemia—serum potassium <3.6 mmol/L; hyperkalemia—serum potassium >5.1 mmol/L; elevated serum creatinine—serum creatinine >113umol/L for male patients 19 years old and above, >91umol/L for female patients 19 years old and above, or elevated serum creatinine according to the age- and sex-specific pediatric reference intervals for biochemical markers by Colantonio, et al.[18] for patients below 19 years old; low serum creatinine—serum creatinine <57umol/L for male patients 19 years old and above, <39umol/L for female patients 19 years old and above, or low serum creatinine according to the age- and sex-specific pediatric reference intervals for biochemical markers by Colantonio, et al.[18] for patients below 19 years old; and unmet urine output (<0.05cc for adult patients or <0.1cc for pediatric patients). We also defined major burns as burn injuries involving a total of >25% TBSA with partial-thickness or 2-10% TBSA with full-thickness injuries for adult patients, or a total of >20% TBSA with partial-thickness or 2-10% TBSA with full-thickness injuries for pediatric patients.

The main outcome measures for this study were prolonged hospital stay (>30 days), presence of sepsis, and death. Sepsis was considered in a patient when exaggerated cardinal signs of inflammation (i.e., redness, increased heat, swelling, pain, and loss of function) were observed in any part of the burn wounds, with the presence of two or more of the following: hypotension (SBP <90mmHg or a fall of >40mmHg from baseline or less than 2 standard deviations below normal for age in the absence of other causes of hypotension, or a mean arterial pressure of <70mmHg), serum lactate >1mmol/L, mottled skin, decreased capillary refill of nail beds or skin, fever of >38.3°C core temperature, hypothermia of <6°C core temperature, heart rate >90 bpm, tachypnea, change in mental status, significant edema or positive fluid balance (>20 mL/kg over 24 hours), hyperglycemia (>140 mg/dL for patients without history of DM), WBC count >12x10^3/uL or <4x10^3/uL or with >10% immature forms, elevated C-reactive protein, elevated procalcitonin, arterial hypoxemia (PaO2/FiO2 <300), acute drop in urine output (<0.5 mL/kg/hr for at least 2 hrs or 35 mL/hr for a 70-kg person), increase of >0.5 mg/dL in creatinine, international normalized ratio of >1.5 or activated partial thromboplastin time >60 seconds, absent bowel sounds, platelet count <100,000 x 10^3/uL, and bilirubin >4 mg/dL.[19-21]

Statistical analysis

We summarized continuous variables as means and standard deviations, and compared means using t-test. We summarized categorical variables as frequencies and percentages, and compared proportions using the chi-square test or Fisher's exact test. We also performed univariate logistic regression to determine the unadjusted associations of the selected clinical factors with the presence of sepsis, prolonged hospital stay, and death. We expressed associations of variables as odds ratios (OR) and their 95% confidence intervals. We also did sub-analyses sub-analyses of variable associations within the pediatric subpopulation (<18 years old), as well as within the adult subpopulation (≥18 years old), when enough data were available. We used Epi Info™ 7.2.2.6 for all our statistical tests.

RESULTS

A total of 181 patients, 73 for the RDA group and 108 for the PRK group, were included in the analysis of this study. Table 1 shows the comparison of demographic and clinical profiles of patients in the RDA group and in the PRK group.

Overall, the exposure groups were significantly different in terms of distribution of types of burn (p=0.0082), and

Table 1 Demographic and clinical characteristics of the patients

Characteristics	Overall					Pediatric					Adult				
	n	PRK group	n	RDA group	p-value	n	PRK group	n	RDA group	p-value	n	PRK group	n	RDA group	p-value
Mean age ± SD, *years*	108	24.07 ± 19.78	73	28.11 ± 22.42	0.2036	43	3.02 ± 3.27	25	2.64 ± 2.04	0.6046	65	38.00 ± 12.33	48	41.38 ± 15.60	0.2018
Sex, *frequency (%)*	108		73		0.1125	43		25		0.0049*	65		48		0.8896
Male		80 (74.07)		46 (63.01)			32 (74.42)		10 (40.00)			48 (73.85)		36 (75.00)	
Female		28 (25.93)		27 (36.99)			11 (25.58)		15 (60.00)			17 (26.15)		12 (25.00)	
Types of burn, *frequency (%)*	108		73		0.0082*	43		25		0.1496†	65		48		0.0167*
Thermal		82 (75.93)		68 (93.15)			38 (88.37)		25 (100.00)			44 (67.69)		43 (89.58)	
Electrical		22 (20.37)		5 (6.85)			5 (11.63)		0 (0.00)			17 (26.15)		5 (10.42)	
Chemical		4 (3.70)		0 (0.00)			0 (0.00)		0 (0.00)			4 (6.15)		0 (0.00)	
Burn severity, *frequency (%)*	108		73		0.4037†	43		25		1.0000†	65		48		0.5070†
Partial thickness		103 (95.37)		72 (98.63)			40 (93.02)		24 (96.00)			63 (96.92)		48 (100.00)	
Full thickness		5 (4.63)		1 (1.37)			3 (6.98)		1 (4.00)			2 (3.08)		0 (0.00)	
Comorbidities, *frequency (%)*	108		73			43		25			65		48		
Hypertension		24 (22.22)		22 (30.14)	0.2302		1 (2.33)		0 (0.00)	1.0000†		23 (35.38)		22 (45.83)	0.2621
Diabetes mellitus		6 (5.56)		18 (24.66)	0.0002*†		0 (0.00)		0 (0.00)	--		6 (9.23)		18 (37.50)	0.0003*
Abnormal vital signs, *frequency (%)*															
Hypotensive	100	4 (4.00)	72	3 (4.17)	1.0000†	37	4 (10.81)	24	3 (12.50)	1.0000†	63	0 (0.00)	48	0 (0.00)	--
Hypertensive	100	10 (10.00)	72	7 (9.72)	0.9520	37	4 (10.81)	24	4 (16.67)	0.7004	63	6 (9.52)	48	3 (6.25)	0.7293†
Tachycardic	100	7 (7.00)	73	8 (10.96)	0.3608	39	6 (15.38)	25	7 (28.00)	0.2210	61	1 (1.64)	48	1 (2.08)	1.0000†
Mean Glasgow Coma Score (GCS) ± SD	72	15 ± 0	52	14 ± 1	0.0007*†	12	15	4	15	--	60	15 ± 0	48	14 ± 1	0.0012*
AVPU, *frequency (%)*	36		21			31		21			5		0		
Alert		34 (94.44)		21 (100.00)	0.5263†		29 (93.55)		21 (100.00)	0.5090		5 (100.00)		0 (0.00)	--
Painful stimulation		2 (5.56)		0 (0.00)	0.5263†		2 (6.45)		0 (0.00)	0.5090		0 (0.00)		0 (0.00)	--
Abnormal laboratory parameters, *frequency (%)*															
Leukocytosis	108	45 (41.67)	73	24 (32.88)	0.2323	43	21 (48.84)	25	7 (28.00)	0.0923	65	24 (36.92)	48	17 (35.42)	0.8692
Hyponatremia	107	34 (31.78)	73	29 (39.73)	0.2722	43	12 (27.91)	25	10 (40.00)	0.3040	64	22 (34.38)	48	19 (39.58)	0.5712
Hypernatremia	107	8 (7.48)	73	1 (1.37)	0.0855†	43	3 (6.98)	25	1 (4.00)	1.0000†	64	5 (7.81)	48	0 (0.00)	0.0695†
Hypokalemia	105	44 (41.90)	73	43 (58.90)	0.0256*	43	17 (39.53)	25	16 (64.00)	0.0516	62	27 (43.55)	48	27 (56.25)	0.1863
Hyperkalemia	105	9 (8.57)	73	0 (0.00)	0.0112*†	43	5 (11.63)	25	0 (0.00)	0.1496†	62	4 (6.45)	48	0 (0.00)	0.3842†
Elevated serum creatinine	107	47 (43.93)	73	19 (26.03)	0.0144*	43	40 (93.02)	25	18 (72.00)	0.0307*†	64	7 (10.94)	48	1 (2.08)	0.1348†
Arterial blood gas	99		63			38		22			61		41		
Uncompensated metabolic acidosis		0 (0.00)		6 (9.52)	0.0029*†		0 (0.00)		0 (0.00)	--		0 (0.00)		6 (14.63)	0.0033*†
Uncompensated metabolic alkalosis		3 (3.03)		0 (0.00)	0.2826†		0 (0.00)		0 (0.00)	--		3 (4.92)		0 (0.00)	0.2717†
Mean total body surface area affected ± SD, %	108	17.57 ± 12.22	73	19.08 ± 10.31	0.3860	43	14.63 ± 9.65	25	13.08 ± 8.15	0.5028	65	19.51 ± 13.38	48	22.21 ± 9.98	0.2431
Major burns, frequency (%)	108	27 (25.00)	73	73 (40.33)	0.9583	43	12 (27.91)	25	3 (12.00)	0.2241†	65	15 (23.08)	48	15 (31.25)	0.3308

*significant at p<0.05
†Fisher's exact test

Table 2 Comparison of outcomes

Characteristics	Overall					Pediatric					Adult				
	n	PRK	n	RDA	p-value	n	PRK	n	RDA	p-value	n	PRK	n	RDA	p-value
Mean length of hospital stay ± SD, *days*	108	17.22 ± 20.45	73	11.67 ± 9.69	0.0317*	43	15.51 ± 13.07	25	9.88 ± 9.43	0.0638	65	18.35 ± 24.16	48	12.58 ± 9.79	0.1213
Prolonged hospital stay, *frequency (%)*		13 (12.04)		2 (2.74)	0.0287*†		6 (13.95)		1 (4.00)	0.2482		7 (10.77)		1 (2.08)	0.1351†
Sepsis, *frequency (%)*	102	5 (4.67)	73	0 (0.00)	0.0815†	43	1 (2.33)	25	0 (0.00)	1.0000†	64	4 (6.25)	48	0 (0.00)	0.1336†
Death, *frequency (%)*	108	8 (7.41)	73	2 (2.74)	0.3199†	43	4 (9.30)	25	0 (0.00)	0.2885†	61	4 (6.15)	48	2 (4.17)	1.0000†

*significant at p<0.05
†Fisher's exact test

patients in the RDA group had a significantly higher proportion of patients with DM (18/73, 24.66% vs 6/108, 5.56%; p=0.0002), lower mean GCS (14 ± 1 vs 15 ± 0; p=0.0007), higher proportion of patients with hypokalemia (43/73, 58.90% vs 44/105, 41.90%; p=0.0256), lower proportion of patients with hyperkalemia (0/73, 0.00% vs 9/105, 8.57%; p=0.0112), lower proportion of patients with elevated serum creatinine (19/73, 26.03% vs 47/107, 43.93%; p=0.0144), and higher proportion of patients with uncompensated metabolic acidosis (6/63, 9.52% vs 0/99, 0.00%; p=0.0029). Among pediatric patients,

Table 3 Univariate regression analysis showing the association of patient characteristics and fluid management with patient outcomes among all patients

	Prolonged hospital stay		Sepsis		Death	
Characteristics	**Odds ratio (95% CI)**	**p-value**	**Odds ratio (95% CI)**	**p-value**	**Odds ratio (95% CI)**	**p-value**
Age (>18 years old)	0.67 (0.23 to 1.92)	0.4496	2.48 (0.27 to 22.67)	0.4208	0.90 (0.24 to 3.29)	0.8688
Male sex	0.46 (0.16 to 1.35)	0.1600	0.65 (0.11 to 4.01)	0.6436	4.14 (0.51 to 33.42)	0.1823
Thermal burn	3.09 (0.39 to 24.35)	0.2852	0.83 (0.09 to 7.67)	0.8676	§	§
Electrical burn	0.38 (0.05 to 3.05)	0.3661	1.43 (0.15 to 13.33)	0.7513	§	§
Full-thickness burn injuries	29.80 (4.91 to 180.97)	0.0002*	§	§	10.44 (1.66 to 65.70)	0.0125*
Hypertension comorbidity	0.19 (0.02 to 1.50)	0.1160	13.08 (1.42 to 120.28)	0.0232*	1.28 (0.32 to 5.15)	0.7323
Diabetes comorbidity	0.44 (0.06 to 3.54)	0.4435	1.66 (0.18 to 15.45)	0.6565	0.72 (0.09 to 5.91)	0.7559
Tachycardic	0.74 (0.09 to 6.01)	0.7740	§	§	§	§
Leukocytosis	1.97 (0.68 to 5.69)	0.2111	§	§	4.10 (1.02 to 16.43)	0.0462*
Hyponatremia	1.03 (0.33 to 3.23)	0.9533	7.80 (0.85 to 71.33)	0.0690	0.45 (0.09 to 2.17)	0.3178
Hypernatremia	7.27 (1.60 to 33.07)	0.0102*	§	§	2.25 (0.25 to 20.00)	0.4666
Hypokalemia	0.67 (0.23 to 1.98)	0.4746	1.57 (0.26 to 9.64)	0.6253	0.11 (0.01 to 0.85)	0.0351*
Hyperkalemia	§	§	5.13 (0.51 to 51.29)	0.1644	40.93 (8.37 to 200.19)	<0.0001*
Abnormal creatinine	1.57 (0.54 to 4.55)	0.4040	0.42 (0.05 to 3.83)	0.4413	1.79 (0.50 to 6.42)	0.3727
Uncompensated metabolic acidosis	2.03 (0.22 to 18.61)	0.5316	§	§	§	§
Uncompensated metabolic alkalosis	§	§	§	§	15.40 (1.19 to 199.28)	0.0363*
Major burns	2.17 (0.73 to 6.48)	0.1647	0.74 (0.08 to 6.84)	0.7943	8.17 (2.01 to 33.11)	0.0033*
RDA formula	0.21 (0.05 to 0.94)	0.0417*	§	§	0.35 (0.07 to 1.71)	0.1952

*significant at p<0.05
§Undefined

Table 4 Univariate regression analysis showing the association of patient characteristics and fluid management with patient outcomes among pediatric patients

	Prolonged hospital stay		Death	
Characteristics	**Odds ratio (95% CI)**	**p-value**	**Odds ratio (95% CI)**	**p-value**
Male sex	1.62 (0.29 to 9.03)	0.5817	§	§
Tachycardic	0.63 (0.07 to 5.70)	0.6776	§	§
Leukocytosis	4.13 (0.74 to 23.05)	0.1060	§	§
Hyponatremia	1.66 (0.34 to 8.15)	0.5332	0.68 (0.07 to 6.96)	0.7474
Hypernatremia	44.99 (3.77 to 536.71)	0.0026*	§	§
Hypokalemia	0.39 (0.07 to 2.15)	0.2781	§	§
Hyperkalemia	§	§	20.41 (2.09 to 198.82)	0.0094*
Major burns	6.06 (1.18 to 31.04)	0.0305*	3.93 (0.50 to 30.57)	0.1913
RDA formula	0.26 (0.03 to 2.27)	0.2216	§	§

*significant at p<0.05
§Undefined

the exposure groups were significantly different in terms of distribution of sex (p=0.0049), and those in the RDA group had a significantly lower proportion of patients with elevated serum creatinine (18/25, 72.00% vs 40/43, 93.02%; p=0.0307). Among adult patients, the exposure groups were significantly different in terms of distribution of types of burn (p=0.0167), and those in the RDA group had a significantly higher proportion of patients with DM (18/48, 37.50% vs 6/65, 9.23%; p=0.0003), lower mean GCS (14 ± 1 vs 15 ± 0; p=0.0012), and higher proportion of patients with uncompensated metabolic acidosis (6/41, 14.63% vs 0/61, 0.00%; p=0.0033). No patients from either group were bradycardic or unresponsive to stimulation. Also, no patients from either group had abnormal urine output, leukopenia, uncompensated respiratory acidosis or alkalosis, or low creatinine. The rest of the clinical profiles were comparable between the two groups.

Table 2 shows the comparison of patient outcomes between the two exposure groups. Patients managed with the RDA formula had significantly lower mean length of hospital stay (11.67 ± 9.69 days vs 17.22 ± 20.45 days; p=0.0317), and lower proportion of patients with prolonged hospital stay (2/73, 2.74% vs 13/108, 12.04%; p=0.0287). Other patient outcomes were comparable between the two groups. The outcomes were also comparable between the two exposure groups when analyzed within the pediatric subgroup, as well as within the adult subgroup.

The associations of patient characteristics and fluid management with patient outcomes among all patients are shown in Table 3. Full-thickness burns (OR=29.80; 95% CI 4.91 to 180.97; p=0.0002) and hypernatremia (OR=7.27; 95% CI 1.60 to 33.07; p=0.0102) significantly increased the odds ratio of prolonged hospital stay. Fluid resuscitation using the RDA formula significantly decreased the odds ratio of prolonged hospital stay (OR=0.21; 95% CI 0.05 to 0.94; p=0.0417). Hypertension

Table 5 Univariate regression analysis showing the association of patient characteristics and fluid management with patient outcomes among adult patients

	Prolonged hospital stay		Sepsis		Death	
Characteristics	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value
Male sex	0.18 (0.04 to 0.80)	0.0241*	1.05 (0.10 to 10.51)	0.9670	1.77 (0.20 to 15.75)	0.6100
Thermal burn	2.19 (0.26 to 18.64)	0.4740	1.05 (0.10 to 10.51)	0.9670	§	§
Electrical burn	0.57 (0.07 to 4.90)	0.6114	§	§	§	§
Full-thickness burn injuries	§	§	§	§	§	§
Hypertension comorbidity	0.20 (0.02 to 1.67)	0.1367	§	§	1.5480 (0.2983 to 8.0321)	0.6030
Diabetes comorbidity	0.51 (0.06 to 4.35)	0.5377	1.23 (0.12 to 12.41)	0.8595	0.73 (0.08 to 6.57)	0.7794
Leukocytosis	1.06 (0.24 to 4.67)	0.9404	§	§	1.82 (0.35 to 9.45)	0.4773
Hyponatremia	0.68 (0.13 to 3.66)	0.6505	5.45 (0.55 to 54.14)	0.1480	0.33 (0.04 to 2.93)	0.3195
Hypernatremia	§	§	§	§	5.10 (0.48 to 54.45)	0.1775
Hypokalemia	1.04 (0.25 to 4.39)	0.9574	3.18 (0.32 to 31.53)	0.3237	0.19 (0.02 to 1.71)	0.1389
Hyperkalemia	§	§	§	§	50.91 (6.08 to 426.51)	0.0003*
Elevated creatinine	§	§	§	§	2.83 (0.29 to 27.66)	0.3703
Uncompensated metabolic acidosis	2.54 (0.26 to 24.88)	0.4223	§	§	§	§
Uncompensated metabolic alkalosis	§	§	§	§	16.00 (1.12 to 228.98)	0.0412*
Major burns	0.92 (0.18 to 4.81)	0.9195	0.91 (0.09 to 9.08)	0.9353	16.40 (1.83 to 146.98)	0.0124*
RDA formula	0.18 (0.02 to 1.48)	0.1103	§	§	0.66 (0.12 to 3.78)	0.6436

*significant at p<0.05
§Undefined

Table 6 Multivariable odds ratios (95% CI) for prolonged hospital stay and death among all patients

	Adjusted odds ratio (95% CI)	
Characteristics	Prolonged hospital stay	p-value
Full-thickness burns	28.64 (4.20 to 195.56)	0.0006*
Hypernatremia	5.44 (0.98 to 30.24)	0.0531
RDA formula	0.30 (0.06 to 1.52)	0.1463
	Death outcome	
Full-thickness burns	§	§
Leukocytosis	2.20 (0.33 to 14.85)	0.4165
Hypokalemia	0.16 (0.02 to 1.63)	0.1213
Hyperkalemia	8.22 (0.06 to 1067.56)	0.3963
Uncompensated metabolic alkalosis	3.83 (0.03 to 463.48)	0.5829
Major burns	27.65 (2.69 to 284.25)	0.0052*

*significant at p<0.05
§Undefined

Table 7 MMultivariable odds ratios (95% CI) for prolonged hospital stay among pediatric patients, and death among adult patients

Characteristics	Adjusted odds ratio (95% CI) Prolonged hospital stay (pediatric patients)	p-value
Hypernatremia	106.53 (5.16 to 2200.88)	0.0025*
Major burns	14.02 (1.37 to 143.91)	0.0263*
	Death outcome (adult patients)	
Hyperkalemia	7.51 (0.08 to 699.99)	0.3834
Uncompensated metabolic alkalosis	7.51 (0.08 to 699.99)	0.3834
Major burns	10.66 (0.93 to 122.00)	0.0570

*significant at p<0.05

comorbidity significantly increased the odds ratio of sepsis (OR=13.08; 95% CI 1.42 to 120.28; p=0.0232). Full-thickness burns (OR=10.44; 95% CI 1.66 to 65.70; p=0.0125), leukocytosis (OR=4.10; 95% CI 1.02 to 16.43; p=0.0462), hyperkalemia (OR=40.93; 95% CI 8.37 to 200.19; p<0.0001), uncompensated metabolic alkalosis (OR=15.40; 95% CI 1.19 to 199.28; p=0.0363), and major burns (OR=8.17; 95% CI 2.01 to 33.11; p=0.0033) all significantly increased the odds ratio of death. Hypokalemia, on the other hand, decreased the odds ratio of death (OR=0.11; 95% CI 0.01 to 0.85; p=0.0351).

Table 4 shows the association of patient characteristics and fluid management with patient outcomes among pediatric patients. Hypernatremia (OR=44.99; 95% CI 3.77 to 536.71; p=0.0026) and major burns (6.06; 95% CI 1.18 to 31.04; p=0.0305) significantly increased the odds ratio of prolonged hospital stay. Hyperkalemia (OR=20.41; 95% CI 2.09 to 198.82; p=0.0094) significantly increased the odds ratio of death. The odds ratios of sepsis could not be computed due to inadequate data on the outcome among pediatric patients in the study.

Table 5 shows the association of patient characteristics and fluid management with patient outcomes among adult patients. Being male (OR=0.18; 95% CI 0.04 to 0.80; p=0.0241) significantly decreased the odds ratio of prolonged hospital stay. Hyperkalemia (OR=50.91; 95% CI 6.08 to 426.51; p=0.0003), uncompensated metabolic alkalosis (OR=16.00; 95% CI 1.12 to 228.98; p=0.0412), and major burns (OR=16.40; 95% CI 1.83 to 146.98; p=0.0124) significantly increased the odds ratio of death among adult patients in the study.

All statistically significant variables in the univariate logistic regression analyses were entered into a multiple regression model. The multivariable odds ratios (95% CI) for prolonged hospital stay and death among all patients are presented in Table 6. In this regression model, only having full-thickness burns independently increased the odds ratio of prolonged hospital stay among all patients (adjusted OR=28.64; 95% CI 4.20 to 195.56; p=0.0006). Only having major burns independently increased the odds ratio of death among all patients (adjusted OR=27.65; 95% CI 2.69 to 284.25; p=0.0052).

Among pediatric patients, the multivariable odds ratios (95% CI) for prolonged hospital stay and death are shown in Table 7. Both hypernatremia (adjusted OR=106.53; 95% CI 5.16 to 2200.88; p=0.0025), and major burns (adjusted OR=14.02; 95% CI 1.37 to 143.91; p=0.0263) independently increased the odds ratio of prolonged hospital stay. Among adult patients, none of the variables in the regression model showed significant independent association with death.

DISCUSSION

Key results

In this study, patients with partial- or full-thickness burns who were managed using the RDA formula had a significantly lower mean length of hospital stay and lower proportion of patients with prolonged hospital stay compared to those managed using the PRK formula. Among all the patients in the study, full-thickness burns had positive and independent association with prolonged hospital stay, and major burns had positive and independent association with death. Among pediatric patients, hypernatremia and major burns had positive and independent association with prolonged hospital stay.

Strengths and limitations

With this study, among patients with partial- or full-thickness burns, we were able to establish the advantage of adding sodium bicarbonate—during the fluid resuscitation phase of burn management—in shortening the hospital stay of patients. We were also able to determine the different clinical factors that were associated with prolonged hospital stay, sepsis, and death among all patients included in the study. The results from our separate subanalyses among pediatric patients and among adult patients, however, may have been limited because the subgroup samples from these subanalyses were not powered to draw robust conclusions from their respective data.

Interpretation

Severe burns may induce acid-base changes, with metabolic acidosis being the most common derangement that occurs. Blood pH and base excess values have a decreasing linear association with the percent TBSA with burn injuries, such that significant acidosis is observed within two hours after extensive burns.[22 23] The addition of an alkaline buffering agent, such as sodium bicarbonate, to an isotonic Ringer's lactate—as in the RDA fluid resuscitation approach—produces a hypertonic solution, which may be used for early fluid resuscitation in severe hypovolemia and shock[24] observed in major and deep burns. The use of hypertonic solution for patients with burn injuries decreases the formation of burn edema and abdominal compartment syndrome by reversing fluid shifts.[12 25] Reducing the risks of these complications during burn management would eventually translate into shorter hospital stays.

In our study, early hypernatremia (upon patient admission) was positively associated with prolonged hospital stay, but not with death, in the overall population and in the pediatric subgroup of patients with burn injuries. Dysnatremias are associated with poor outcomes and increased mortality in severe burn injury. The effect of hypernatremia on burn patient outcomes is more significant than hyponatremia.[26] Sepsis and insensible fluid losses, which are often present in severely burned patients, can cause hypernatremia.[27 28] Several studies have shown that hypernatremia is associated with increased mortality rate (30% to 48%) in patients with severe burns.[29 30] Another study has demonstrated that sodium variability in the early phase of burn injury, and not hypernatremia, is associated with death.[26]

Major burns and full-thickness burns have been associated with increased length of hospital stay and mortality.[31 32] Percent TBSA burned, full-thickness burns, and female gender are the strongest predictors influencing length of hospital stay.[33] Similarly, among all the patients in our study, full-thickness burns and major burns were positively and independently associated with prolonged hospital stay and death, respectively. In the first phase of a major burn injury, there is a large intravascular volume loss due to increase in capillary and venular permeability and increase in interstitial osmotic pressure in burn tissues. At the cellular level, burn shock produces a reduced transmembrane potential and a decreased sodium-potassium ATP-ase activity in the cell membrane.[34] This causes a fluid and protein shift from intravascular to interstitial and intracellular spaces. Intracellular water and sodium increases, and extracellular potassium increases.[2 35] Hyponatremia ensues as a result of extracellular sodium depletion, and hyperkalemia occurs due to metabolic acidosis, as well as from the release of potassium from damaged cells,[36] i.e., massive tissue necrosis and cell lysis.[1 4 35] Severe hyperkalemia, in acute burns, can lead to sudden death from cardiac arrhythmias.[37] In our study, hyperkalemia was positively associated with death among all patients.

In addition to acidosis, metabolic alkalosis may also develop, particularly among patients with severe burns. The high-level inflammatory response triggered by severe burn injury causes an increase in adrenocortical activity,[23] bringing about high levels of free plasma cortisol during the early phase of the injury.[38 39] This produces cardiac derangements, which can lead to death.[40 41] The level of free plasma cortisol is directly correlated with percent TBSA with burn injuries.[38]

Generalizability

For this study, we included patients of any age, sex, or clinical condition, who had partial- or full-thickness burns, and who came to our institution within an 11-year span. The profiles of the patients in this study are typical of those who are admitted in hospital burn units. The results of this study may therefore be applied to most patients admitted for burn management.

CONCLUSION

In this retrospective cohort study among patients with partial- or full-thickness burns, we found out that patients managed using the RDA formula had significantly shorter hospital stay. We also found out that full-thickness burns and major burns had positive and independent association with prolonged hospital stay and death, respectively.

Contributors
RDRM, BEV, RDA, FJMG and ASC had substantial contributions to the study design, and to the acquisition, analysis and interpretation of data. RDRM wrote the original draft and subsequent revisions, and reviewed, edited, and approved the final version of the manuscript. All authors agreed to be accountable for all aspects of the work.

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This study was reviewed and approved by the Department of Health XI Cluster Ethics Review Committee (DOH XI CERC reference P19062801).

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