Impact of Burn Size and Initial Serum Albumin Level on Acute Renal Failure Occurring in Major Burn

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Key Words

Acute renal failure · Burn · Albumin · Burn size · Mortality

Abstract

Background: Acute renal failure (ARF) is not a rare occurrence in severe burns and is an important complication leading to an increase in mortality. The severity of the burn is largely determined by the burn size, and severe burns are likely to cause enough loss of extracellular fluid and albumin from plasma volume to produce shock and hypoalbuminemia. **Hypothesis:** We hypothesized that initial serum albumin level may be useful as an indicator of prognosis and severity of injury in burned patients. **Methods:** The clinical characteristics of 147 adult patients with second- and third-degree burns covering 30% or more of their body surface area were analyzed retrospectively. Logistic regression was used to estimate the relative risks of ARF and mortality associated with the larger burn size and the lower serum albumin level at admission. **Results:** Mean burned body surface was $60.0 \pm 21.8\%$ (range 30–100%). Twenty-eight

(19.0%) out of 147 patients experienced ARF, defined as a serum creatinine ≥ 2 mg/dl, during the admission. The patients with ARF had larger burn size (79.5 ± 15.4 vs. $55.3 \pm 20.5\%$, $p < 0.0001$) and lower serum albumin concentration at admission (1.92 ± 0.66 vs. 2.48 ± 0.82 g/dl, $p < 0.0005$) compared with those without ARF. All patients with ARF expired, whereas 29.4% (35/119) of the patients without ARF died. The burn size $\geq 65\%$ was associated with a risk of ARF that was 9.9 times and with a risk of death that was 14.2 times as high as that for the burn size $< 65\%$. The initial serum albumin level < 2.5 g/dl was associated with a risk of death that was 2.7 times as high as that for the initial serum albumin level ≥ 2.5 g/dl. **Conclusions:** When major burns are complicated by ARF, the mortality rate increases significantly. Burn size is an independent predictor of ARF occurring in major burns. Initially depressed serum albumin level is associated with an increase in mortality in the major burn patients.

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Introduction

Acute renal failure (ARF) in burns is not a rare occurrence, and the prognosis of burned patients with ARF is known to be grave. The incidence of ARF in burned patients has been reported to vary from 1 to 30%, with the mortality in these patients ranging from 73 to 100% [1–3]. Despite improved management and the availability of dialytic support, mortality rates in burned patients with ARF have remained above 80% [4, 5]. Therefore, whether burn injury is complicated by ARF is very important in patient survival.

Since the severity of the burn is largely determined by the burn size, the burn size would be the limiting factor to survive the thermal injury [6]. It is also conceivable that the occurrence of ARF in burns should depend on the severity of the burns. Holm et al. [7] recently reported a correlation between the burn size and the development of ARF in patients with burns >10% body surface area.

Two important factors contributing to the occurrence of ARF in burns are initial hypovolemia and later sepsis [4, 7, 8]. Burns affecting more than 20% of skin surface are likely to cause enough loss of extracellular fluid and albumin from plasma volume to produce shock and hypoalbuminemia [9]. The ARF occurring in the first few days after the thermal injury is related to intravascular volume depletion [10]. In addition, hypoalbuminemia may result in impaired wound healing [11], predisposing to sepsis. However, it has not been clear whether hypoalbuminemia itself can be used as an independent predictor of ARF or mortality in major burns.

This study was focused on the prognosis of ARF occurring in major burns. 'Major' burns here refer to second- and third-degree burns involving 30% or more of body surface area. By analyzing the clinical course of ARF occurring in major burn patients, we investigated the impact of burn size and initial serum albumin level on the occurrence of ARF and patient survival in major burns.

Patients and Methods

The records of 176 acutely burned patients were reviewed. All patients were admitted from January 1, 2000 to December 31, 2000 to the burn intensive care unit at the Hallym University Hangang Sacred Heart Hospital in Seoul, Korea. Of these, the adult (>15 years of age) patients with second- and third-degree burns covering 30% or more of their body surface area were enrolled. Excluding a few patients with chronic renal failure, 147 patients were subjected to this retrospective analysis.

The following clinical data were collected: age, sex, type of burn, burn size, initial serum albumin concentration (at the time of admis-

sion), serial blood urea nitrogen (BUN) and serum creatinine levels, presence or absence of oliguria (<500 ml/d), duration of hospitalization and factors related to the ARF. Specifically, presence or absence of significant hypotension (mean arterial pressure <60 mm Hg for more than 2 h) and sepsis (defined as evidence of infection with a systemic response), requirement of ventilatory support and the use of potentially nephrotoxic agents (aminoglycosides, vancomycin, amphotericin B and nonsteroidal anti-inflammatory drugs) were considered. Information regarding the time of occurrence and causes of ARF, mortality and causes of death were also collected. ARF was defined as an elevation of the serum creatinine level to 2 mg/dl or more during the admission, considering a possible increase in creatinine release from muscles in burned patients. At admission all burned patients were resuscitated with fluid therapy according to the Parkland's formula [12].

Continuous data were described as means $\pm$ SD. Statistical comparisons between the groups were performed using Mann-Whitney U test, and correlations between variables of interest were analyzed by linear regression. $p < 0.05$ were considered as indicative of statistical significance.

Categorical data were analyzed using contingency tables and χ^2 test. Burn size was analyzed as both continuous and categorical (<65 and $\geq 65\%$) predictors of the risk of ARF and mortality. Initial serum albumin concentration was also analyzed as both continuous and categorical (<2.5 and ≥ 2.5 g/dl) predictors of the risk of ARF and mortality. The cutoff levels dividing the patients into two groups of burn size or initial serum albumin were determined based on the frequency distribution data. Logistic regression was used to model odds ratios and 95% confidence intervals as measures of the association between predictors and outcomes (SPSS for Windows; SPSS Inc., Chicago, Ill., USA).

Results

General Characteristics of the Patients

A total of 147 patients were entered into the study. There were 106 men and 41 women with a mean age of 43.2 ± 14.1 years (range 16–87). Mean second- or third-degree burned body surface, as evaluated upon arrival, was $60.0 \pm 21.8\%$ (range 30–100%) of the total body surface area. One hundred twenty-seven patients had sustained flame burns, 10 were scalds, 8 electric burns and 2 chemical burns.

Twenty-eight out of 147 patients experienced ARF, defined as a serum creatinine ≥ 2 mg/dl, during the admission. Thus, the incidence of ARF in our major burn patients was 19.0%. Sixty-three out of 147 patients died, corresponding to the total mortality rate of 42.9%. Major causes of death were septic shock, acute respiratory distress syndrome and burn shock.

Characteristics of the Patients with ARF

ARF occurred a mean of 6.8 days (range 1–36) after admission. At the time of ARF, 14 patients (50%) were

oliguric. During the admission, BUN reached 55.7 ± 29.2 mg/dl and serum creatinine 4.08 ± 3.04 mg/dl. Oliguric ARF patients had higher peak BUN level compared with nonoliguric ARF patients (65.7 ± 24.8 vs. 45.7 ± 30.7 mg/dl, $p < 0.05$), but peak creatinine level was not different between the two groups (4.36 ± 3.07 vs. 3.79 ± 3.09 mg/dl). The major contributors preceding the ARF were usually multifactorial: significant hypotension (burn shock), rhabdomyolysis, sepsis and use of aminoglycosides. Whereas the ARF associated with significant hypotension or rhabdomyolysis occurred during the first week of admission, the ARF associated with sepsis or use of aminoglycosides occurred thereafter.

Clinical parameters at admission were compared between the patients with ARF and those without ARF (table 1). Age and sex distribution had no differences between the two groups. Most of our patients had flame burns and we could not find any difference according to the burn types. The patients with ARF had larger burn size compared with those without ARF (79.5 ± 15.4 vs. $55.3 \pm 20.5\%$, $p < 0.0001$). The patients with ARF had lower serum albumin concentration at admission compared with those without ARF (1.92 ± 0.66 vs. 2.48 ± 0.82 g/dl, $p < 0.0005$).

Table 2 shows comparisons of the parameters during the admission between the two groups. As expected, episodes of significant hypotension, sepsis and requirement of ventilatory support were more frequent in the patients with ARF than in those without ARF. Notably, all the patients with ARF expired whereas 29.4% (35/119) of the patients without ARF died. Shorter duration of hospitalization in the patients with ARF (11.3 ± 7.9 vs. 64.4 ± 63.3 days, $p < 0.0001$) seemed to be related with this higher mortality. In only 3 patients, renal replacement therapy using intermittent hemodialysis or continuous venovenous hemofiltration was performed. The indication for renal replacement therapy in these patients was progressive azotemia accompanying pulmonary edema. Patient survival was not affected by the application of renal replacement therapy.

Risks of ARF and Death

Figure 1 shows a clear tendency that ARF occurred more frequently in the patients with a larger burn size and those with a lower initial serum albumin level. We evaluated the relative risks of ARF associated with age ≥ 45 years, male sex, burn size $\geq 65\%$ and initial serum albumin < 2.5 g/dl (table 3). The incidence of ARF was not associated with age or sex. The burn size $\geq 65\%$ body surface area was associated with a risk of ARF that was 9.9

Table 1. Comparisons of parameters at admission between patients with and without ARF

	With ARF (n = 28)	Without ARF (n = 119)
Age, years	41.9 ± 13.2	43.5 ± 14.4
Sex ratio, M:F	22:6	84:35
Burn type		
Flame	25	102
Scald	1	9
Electric	1	7
Chemical	1	1
Burn size, %	79.5 ± 15.4	$55.3 \pm 20.5^{**}$
Serum albumin, g/dl	1.92 ± 0.66	$2.48 \pm 0.82^*$

Continuous variables are presented as mean $\pm$ SD. * $p < 0.0005$; ** $p < 0.0001$.

Table 2. Comparisons of parameters during the admission between patients with and without ARF

	With ARF (n = 28)	Without ARF (n = 119)
Significant hypotension	22	31**
Sepsis	27	75*
Septicemia	6	29
Requirement of ventilatory support	27	40**
Peak BUN, mg/dl	55.7 ± 29.2	$17.2 \pm 9.09^{**}$
Peak serum creatinine, mg/dl	4.08 ± 3.04	$1.01 \pm 0.31^{**}$
Duration of hospitalization, days	11.3 ± 7.9	$64.4 \pm 63.3^{**}$
Death	28	35**

Continuous variables are presented as mean $\pm$ SD. * $p < 0.001$; ** $p < 0.0001$.

times as high as that for the burn size $< 65\%$ in multivariate analysis. The initial serum albumin level < 2.5 g/dl was associated with increased risk of ARF in univariate analysis but not significant in multivariate analysis. Thus, the initial serum albumin level did not seem to be an independent predictor of ARF, as reflected by its correlation with the burn size ($p < 0.0001$, fig. 2).

Figure 3 shows a clear tendency of increasing mortality in the patients with a larger burn size and those with a lower initial serum albumin level. We estimated the relative risks of death associated with age ≥ 45 years, male sex, burn size $\geq 65\%$ and initial serum albumin < 2.5 g/dl (table 4). The risk of death was not affected by age or sex. The burn size $\geq 65\%$ body surface area was associated

Fig. 1. Incidence of ARF according to burn size (a) and serum albumin concentration (b) at admission.

Fig. 3. Mortality according to burn size (a) and serum albumin concentration (b) at admission.

Fig. 2. Correlation between burn size and serum albumin concentration at admission.

with a risk of death that was 14.2 times as high as that for the burn size $<65\%$ in multivariate analysis. The initial serum albumin level <2.5 g/dl was also associated with a risk of death that was 2.7 times as high as that for the initial serum albumin level ≥ 2.5 g/dl in multivariate analysis.

Discussion

In this retrospective study of 147 patients seen over a 1-year period at single burn unit, we showed that about one-fifth of the major burn ($\geq 30\%$ body surface area) patients is complicated by ARF (serum creatinine ≥ 2.0 mg/dl) and that the combination of major burn and ARF is invariably fatal. Considering most of our patients with ARF were septic and in the need of ventilatory support, the presence of multiple organ failure should be the main reason why they could not survive.

Table 3. Odds ratios for ARF in major burns associated with the parameters at admission

	Univariate analysis		Multivariate analysis	
	odds ratio	95% CI	odds ratio	95% CI
Age $\geq$ 45 years	0.84	0.37–1.94	0.94	0.37–2.35
Male sex	1.53	0.57–4.09	1.88	0.64–5.50
Burn size $\geq$ 65%	11.9	3.85–36.5	9.87	2.86–34.1
Serum albumin $<$ 2.5 g/dl	4.13	1.56–10.9	1.59	0.51–4.99

Table 4. Odds ratios for patient survival in major burn associated with the parameters at admission

	Univariate analysis		Multivariate analysis	
	odds ratio	95% CI	odds ratio	95% CI
Age $\geq$ 45 years	1.23	0.64–2.37	1.72	0.71–4.15
Male sex	0.82	0.40–1.70	1.02	0.40–2.63
Burn size $\geq$ 65%	19.2	8.32–44.4	14.2	5.71–35.2
Serum albumin $<$ 2.5 g/dl	6.64	3.15–14.0	2.65	1.06–6.64

The above results appear compatible with the recent report by Holm et al. [7], in which the incidence of ARF was 14.6% in 328 patients with burns $>$ 10%. Whereas they reported a mortality rate of 85% in the ARF patients with a mean burned surface area of 48%, our ARF patients had a mean burned surface area of 80%. Our data may have great potential because we analyzed on a large group of patients with more serious burns. We believe that it is probably not possible to study such an amount of patients elsewhere.

We evaluated which parameters at admission were associated with increased risk of ARF and death in the major burn patients. The burn size is clearly a predictive factor of patient survival in burns [6, 13]. We confirmed this notion and the impact of burn size on the occurrence of ARF in major burns as well. The patients with ARF had a mean burned surface area of 80%, while those without ARF had 55%. The risk of ARF was increased with the burn size $\geq$ 65% body surface area 9.9 times as high as that for the burn size $<$ 65%. The incidence of ARF was not associated with age or sex. Contrary to previous reports [13, 14], advancing age and female sex did not increase the risk of death in our patients. A drawback in this retrospective analysis is that inhalation injury could not have been taken into account, considering the prognostic significance of inhalation injury reported by others [13–15].

We hypothesized that serum albumin level may be useful as an indicator of prognosis and severity of injury in

burned patients. Burn injury to skin initiates an intense inflammatory response and release of vasoactive agents, increasing capillary permeability to fluid, albumin and even larger proteins at the burn site [16]. This process reaches its peak in 12–24 h. Albumin has clearly been shown to leak from the intravascular space during at least the first 6–18 h after injury [17, 18]. Besides, examination of the livers of burned animals reveals that the messenger RNA for albumin is decreased in response to injury [19, 20], a response that is associated with the increase in acute phase reactants. After burn shock, therefore, serum albumin levels would continue to decrease because of decreased production and ongoing losses through the wound.

Depressed serum albumin levels at admission have been found to be predictors of higher complication rates for patients with varying clinical problems [11]. In burned patients, the degree of burn involvement may be reflected by the serum albumin concentration at admission. In this context, we showed a significant correlation between burn size and serum albumin level at admission (fig. 2). In addition, depressed serum albumin level at admission was associated with increased risk of ARF and death in univariate analysis. According to the multivariate analysis, however, the initially depressed serum albumin level was not an independent predictor of ARF but an independent predictor of death in the major burn patients. It is probable that serum albumin level at admission may be determined by not only the degree of thermal injury but

also premorbid conditions. Therefore, patient survival might have been affected by premorbid conditions.

In this study, only a few of the patients were dialyzed. Because of the small number of the dialyzed patients, we could not conclude whether renal replacement therapy brought about any benefit in patient survival. Although only 6 patients out of 28 with ARF had their serum creatinine >5 mg/dl, we cannot but admit that burn surgeons in our unit were not very much aware of the need of early dialysis and that the nephrologists involved were not very persuasive in applying renal replacement therapy to those multiorgan failure patients. The prognosis might have been improved with early aggressive application of renal replacement therapy [7, 8, 21].

We conclude that major burns, if complicated by ARF, could be fatal. The risks of ARF and mortality may be predetermined at admission. We cannot be too eager in early fluid resuscitation in major burns. Further studies are required to verify whether patient survival can be improved with early aggressive application of renal replacement therapy in major burn patients.

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