ORIGINAL ARTICLE

Mortality in Burned Children With Acute Renal Failure

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Background: During the past 13 years, mortality from acute renal failure in burned children has been on the decline.

Objective: To determine which new burn therapies contributed to the decrease in mortality.

Design: The medical records of burned children admitted from February 1966 to January 1997 were reviewed, and the outcome of changes in the treatment of burned children were compared.

Patients and Methods: Sixty children with acute renal failure were identified. These children were divided into those admitted from 1966 to 1983 (n = 24) and those admitted from 1984 to 1997 (n = 36). They were compared with matched control subjects from the same period without renal failure. Values are presented as means ± SEMs. Statistical analysis was by the Student *t* test or χ^2 analysis.

Results: Mortality rates in burned children with acute renal failure decreased from 100% before 1983 to 56% after 1984 ($P<.001$). The time between a burn injury and the initiation of intravenous fluid resuscitation was 8.6 ± 1.7 hours before 1983 compared with 3.0 ± 0.5 hours after 1984 ($P<.005$). The time between a burn injury and complete early wound excision decreased from 228 ± 37 hours before 1983 to 40 ± 7 hours after 1984 ($P<.001$). The incidence of sepsis decreased from 71% to 44% in these periods ($P<.05$). After 1984, survivors had a shorter time delay for fluid resuscitation than nonsurvivors (1.7 ± 0.5 hours vs 4.8 ± 0.9 hours; $P<.005$) and a lower incidence of sepsis (19% vs 60%; $P<.05$). From 1984 to 1997, burned children with acute renal failure who did not require dialysis had significantly shorter delays for fluid resuscitation (2.2 ± 0.5 hours vs 4.4 ± 0.9 hours) and complete wound excision (29 ± 6 hours vs 49 ± 7 hours) compared with those requiring dialysis ($P<.05$ for both).

Conclusion: Early adequate fluid resuscitation, early wound excision, and better infection control may reduce mortality in burned children with acute renal failure.

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EXTENSIVE BURN injuries encompass not only the cutaneous wound but also systemic changes associated with serious pathophysiological complications, one of which is acute renal failure.[1] The incidence of acute renal failure in burn patients has been shown to vary widely from 1% to 30% and is associated with a 73% to 100% mortality.[2-5] Before 1965, there were no reported survivors in patients with burn injuries and concomitant acute renal failure. Although survival rates have improved, the prognosis remains poor.[2-4,6]

Acute renal failure is defined as an abrupt decrease in the glomerular filtration rate caused by intrinsic parenchymal disease or alterations in intrarenal hemodynamics. Its major manifestation is the accumulation of waste products (eg, urea, creatinine, and potassium) in the blood. Acute renal failure that occurs immediately after burns is generally due to hypovolemia related to extensive fluid losses from the burn wound, a fluid shift from the circulation into the interstitial or intracellular space, or a delay in fluid resuscitation. Elevated levels of stress-related hormones also cause vasoconstriction, fluid retention, and renal hypoperfusion with tubular necrosis leading to acute renal failure.[7,8] The later appearance of acute renal failure is mainly associated with systemic sepsis[9] and is usually accompanied by other organ failure.[10] The administration of nephrotoxic antibiotics, such as aminoglycosides, and certain cephalosporins that are often used in treating burn infections is also a factor that may cause acute renal failure.[5]

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PATIENTS AND METHODS

Between February 1966 and January 1997, nearly 5000 burned children were admitted to our institution. From these, 60 were identified with acute renal failure as a discharge diagnosis, defined as oliguria for at least 36 hours (urine output <0.5 mL/kg of body weight per hour), a serum urea nitrogen–creatinine ratio of less than 20, a serum creatinine level greater than 177 µmol/L (>2 mg/dL), or any combination of these 3 criteria. Possible contributing factors to mortality, such as patient characteristics, burn size, time from burn to fluid resuscitation, time from burn to wound excision, incidence of sepsis, and the type and duration of dialysis, were evaluated. In this study, "sepsis" was defined as a blood culture revealing the pathogen during the hospital stay or at autopsy.

Burn patients with acute renal failure were divided into 2 groups corresponding to burn care changes at our institution: those admitted from February 1966 to December 1983 (n = 24) and those admitted from January 1984 to January 1997 (n = 36). For further comparisons with the acute renal failure groups, burned children admitted to our institution from 1966 through 1983 and from 1984 through 1997 were randomly selected from children matched by age and burn size in whom acute renal failure did not develop. Patients with acute renal failure in the 1984 to 1997 group were further divided into survivors and nonsurvivors and those who required or did not require dialysis (**Figure 1**). Differences in the delay of fluid resuscitation, the time between burn and wound excision, incidence of sepsis, required dialysis, and mortality rates were compared.

All values in the tables and figures are expressed as means ± SEMs or percentages. Each variable was tested for differences between groups by the Student *t* test or χ^2 analysis where appropriate. Statistical significance was set at $P<.05$.

During the past 13 years at the Shriners Burns Institute, Galveston, Tex, we observed a decrease in mortality in burned children with acute renal failure. We hypothesized that this decrease in mortality is due to new and improved burn therapies. Major changes in therapeutic protocols at our institution occurred from 1983 to 1984. Beginning in 1983, efforts were made to reduce the time from receiving a burn injury to the start of intravenous fluid resuscitation and to hospital admission. In addition, the treatment of burn wounds evolved from a conservative delayed treatment to complete early wound excision. Changes in antibiotic therapy also occurred at this time, when a regimen of gentamicin sulfate plus piperacillin sodium was replaced by that of amikacin sulfate and piperacillin sodium plus vancomycin hydrochloride, which remains the standard perioperative antibiotic protocol at our institution. These therapeutic changes were thought to be related to the decrease in mortality that was observed more than a decade ago in burned children with acute renal failure. To test this hypothesis, burned children identified with acute renal failure were studied for the beneficial effects on mortality of early fluid resuscitation, early wound excision, and changes in antibiotic therapy.

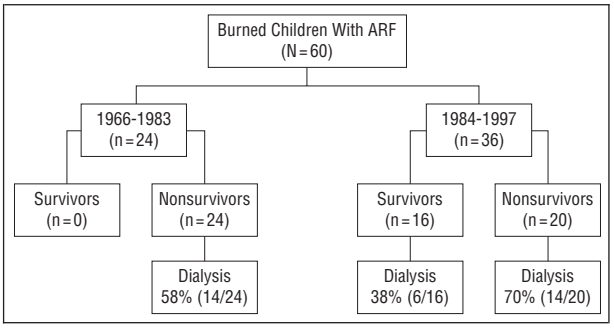

Figure 1. *Patients identified with acute renal failure (ARF) from 1966 to 1997 (N = 60) were divided into those admitted from 1966 to 1983 (n = 24) and those admitted from 1984 to 1997 (n = 36). The 1984-1997 group was subdivided into survivors (n = 16) and nonsurvivors (n = 20). Those requiring dialysis are shown as the percentage of survivors or nonsurvivors.*

RESULTS

Between February 1966 and January 1997, 60 children were identified with acute renal failure. Twenty-four were identified between February 1966 and December 1983 and 36 between January 1984 and January 1997. No significant difference in patient characteristics or burn severity could be shown between these 2 groups and the matched groups without acute renal failure (**Table 1**). In all 60 children, acute renal failure showed a binomial distribution, with 1 peak occurring in the first week after a burn and another 19 to 23 days after a burn. No difference in the time of the onset of acute renal failure could be shown between the groups (**Figure 2**). From 1966 to 1983, the mortality for burned children with acute renal failure was 100%, whereas the mortality for burned children with acute renal failure from 1984 to 1997 decreased to 56% ($P<.001$). The mean time between receiving the burn injury and the start of intravenous fluid resuscitation, the time between burn and wound excision, and the incidence of sepsis are shown in **Table 2**.

To define the characteristics of acute renal failure and to determine whether changes in protocol were associated with improved survival outcome, patients from 1984 to 1997 were divided into survivors and nonsurvivors (there were no survivors from 1966-1983). These 2 subgroups were compared for the same contributing factors. Of 36 children with acute renal failure, 16 survived. No significant differences in age, sex, burn size, or severity of burn injury were found between survivors and nonsurvivors. The mean time between receiving the burn injury and the start of intravenous fluid resuscitation and the incidence of sepsis are depicted in **Figure 3** and **Figure 4**. The time between burn injury and wound excision was 45 ± 8 hours for nonsurvivors and 33 ± 8 hours for survivors ($P = .40$). The mean time delay in fluid resuscitation from 1966 to 1975, 1976 to 1983, and 1984 to 1997 are depicted in **Figure 5**. The mean time between burn injury and the initiation of fluid resuscita-

Table 1. Characteristics of Burned Children With and Without Acute Renal Failure (ARF) From 1966 to 1997*

	1966-1983		1984-1997	
Characteristic	With ARF	Without ARF	With ARF	Without ARF
Patients, No.	24	24	36	36
Age, y	7.8 ± 1.1	7.3 ± 1.0	7.3 ± 0.9	6.4 ± 0.8
Sex, F/M	8/16	7/17	8/28	13/23
TBSA burn, %	70 ± 3	69 ± 3	67 ± 3	70 ± 4
Third-degree TBSA burn, %	66 ± 4	63 ± 3	63 ± 4	64 ± 4

*Except where noted, data are presented as means ± SEMs. No significant differences could be shown between groups. TBSA indicates total body surface area.

Table 2. Delay in Fluid Resuscitation, Time of Wound Excision, and Incidence of Sepsis in Burned Children With and Without Acute Renal Failure (ARF) From 1966 to 1997*

	1966-1983		1984-1997	
Variable	With ARF	Without ARF	With ARF	Without ARF
Delay in fluid resuscitation, h	8.7 ± 1.7†‡	1.5 ± 0.4	3.3 ± 0.6‡	0.9 ± 0.4
Time of wound excision, h	228 ± 35†‡	113 ± 15	41 ± 7	57 ± 7
Incidence of sepsis, %	71†‡	38	44‡	17
Mortality, %	100†‡	33	56‡	14

*Except where noted, data are presented as means ± SEMs.
†Difference between ARF groups: P<.05.
‡Difference between with ARF and without ARF groups: P<.05.

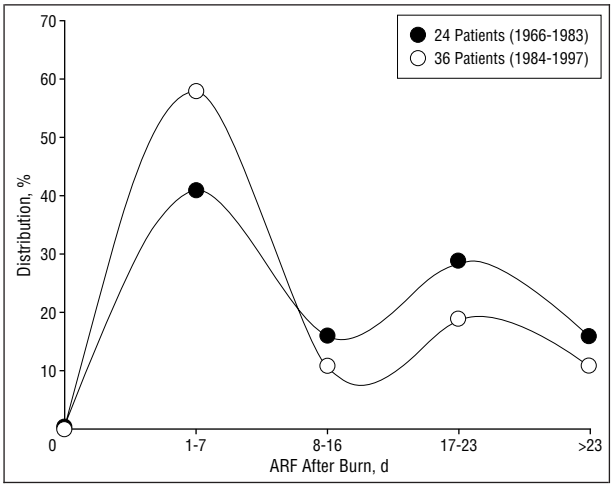

Figure 2. *The time of acute renal failure (ARF) after burn injury. Acute renal failure occurred in a binomial distribution, either 1 to 7 days or 19 to 23 days after burn. No difference in the times of the onset of ARF could be shown between groups.*

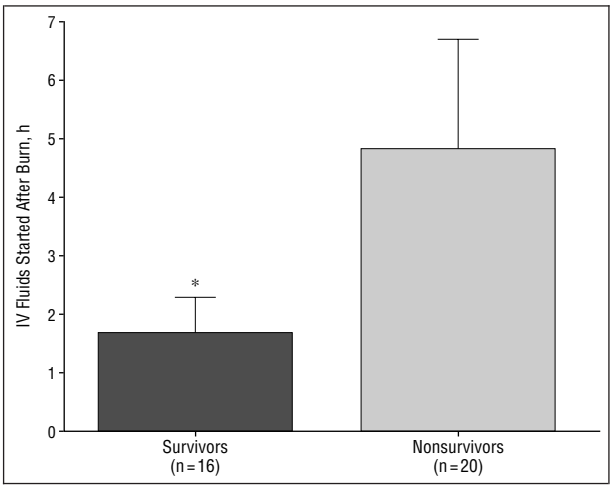

Figure 3. *The time from burn injury to the start of intravenous (IV) fluid resuscitation for survivors vs nonsurvivors from 1984 to 1997. Asterisk indicates significance at* P<.001.

tion decreased from a mean of 15 hours (1966-1975) to a mean of 5 hours (1976-1983), but no significant improvement in survival outcome was noted. It was only when the mean time between the burn injury and starting the intravenous fluid was less than 2 hours that a significant improvement in survival rate could be shown (Figure 5). The 2 groups with acute renal failure were significantly different ($P<.05$) when compared with those without acute renal failure, except for the time of wound excision from 1984 through 1997.

From 1966 to 1983, 14 of 24 children with acute renal failure received dialysis, 13 children by peritoneal dialysis and 1 by peritoneal dialysis and hemodialysis. The mean duration of dialysis in this group was 4.0 ± 1.5 days. From 1984 to 1997, 20 of 36 children with acute renal failure received dialysis, 18 by peritoneal exchange, 1 by peritoneal dialysis and hemodialysis, and 1 by hemodialysis only. The mean duration of dialysis was 5.6 ± 1.5 days. No difference between those with and without dialysis treatment could be shown for patient or injury characteristics, duration of dialysis, or type of dialysis. For children who received dialysis, mortality decreased from 100% from 1966 to 1983 to 62% for those from 1984 to 1997 ($P<.05$). None of the survivors required long-term dialysis treatment.

To define the severity of acute renal failure and the characteristics of dialysis associated with survival, 36 patients from 1984 to 1997 were divided into those who required dialysis and those who did not require dialysis. These 2 subgroups were compared for the factors contributing to acute renal failure. Mortality in patients receiving dialysis was 70% compared with 38% in patients not receiving dialysis ($P = .80$). The mean time delay from burn injury to the start of intravenous fluid resuscitation was significantly higher in those receiving dialysis compared with those not receiving dialysis (4.4 ± 0.9 hours vs 2.2 ± 0.5 hours; $P<.05$). In those requiring dialysis, wound excision was performed 49 ± 7 hours after receiving a burn injury, whereas in those not receiving dialysis, it was 29 ± 6 hours after injury ($P<.05$). The incidence of sepsis in patients requiring dialysis was 60% compared with 38% in patients not requiring dialysis ($P = .30$).

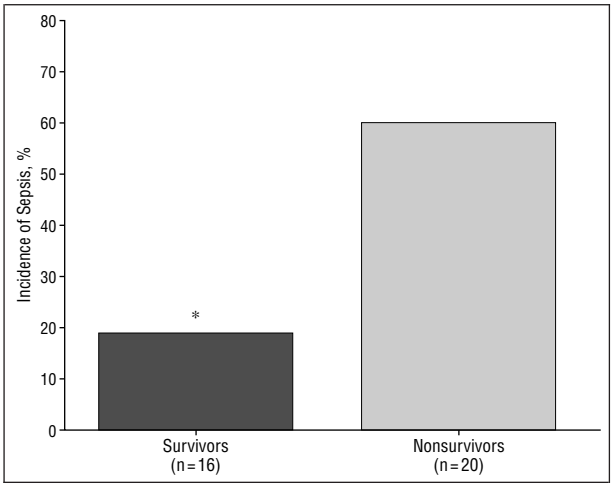

Figure 4. *The incidence of sepsis from 1984 to 1997 for survivors compared with nonsurvivors. Asterisk indicates significance at* P<*.002.*

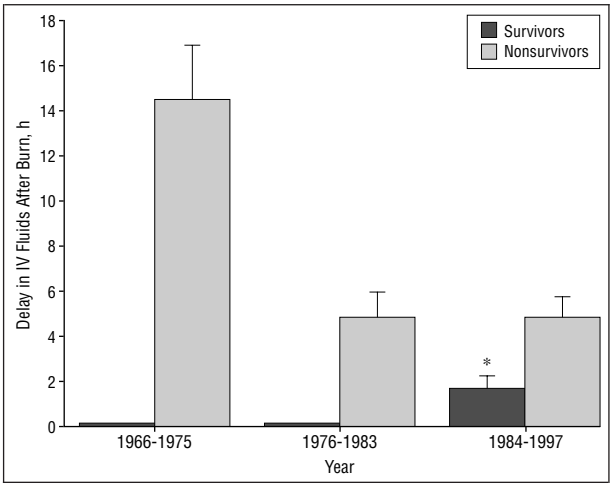

Figure 5. *Before 1983, the mean ± SEM intravenous (IV) fluid resuscitation delay from 1966 to 1975 was 14.0 ± 2.4 hours, and from 1976 to 1983 it was 4.8 ± 1.2 hours. Even with this decrease in the time delay for IV fluid resuscitation, no significant improvement in survival rate was noted. When the mean time from burn injury to the start of the IV fluid resuscitation was less than 2 hours, however, a significant improvement in survival outcome (* P<*.001 [asterisk]) could be demonstrated.*

COMMENT

Mortality in children with burns has decreased during the past 20 years. Improvements in survival rates have been related to new resuscitation techniques, improved wound coverage, better infection control, and advances in critical care. In this report, we showed that mortality associated with renal failure decreased, and this was correlated with major changes in burn therapy that were instituted in 1984. Indeed, mortality associated with acute renal failure decreased at our institution from 100% before 1983 to 56% from 1984 through 1997.

Renal failure in burned children in both periods occurred either immediately after the injury or later when sepsis developed. Acute renal failure occurring immediately after a burn is thought to be due to a decrease in renal perfusion resulting from hypovolemia with extensive fluid losses from the burn wound and a fluid shift from the circulation into the interstitial space. A delay in resuscitation can accentuate the low volume circulation. The decrease in renal blood flow with inadequate resuscitation causes oliguria.[7] Furthermore, it has been shown that burn stress and its associated circulatory derangement stimulate the release of stress-related hormones, such as catecholamines, angiotensin II, aldosterone, and vasopressin.[7,10] These hormonal changes cause vasoconstriction and changes in regional blood flow, particularly in the kidneys.[11] Animal and clinical studies have demonstrated that burn shock manifests lesions in the renal tubules and glomeruli with high- and low-molecular-weight proteins appearing in the urine.[7,8] The later appearance of acute renal failure is mainly associated with systemic sepsis[9] and is usually accompanied by other organ failure such as pulmonary insufficiency, liver failure, or disseminated intravascular coagulopathy.[10] This is a period that is associated with an increase in serum levels of cytokines (tumor necrosis factor, interleukin 1, etc), eicosanoids (prostaglandins, thromboxane, and leukotrienes), and platelet-aggregating factor, among others. All these factors are also produced and released in the early postburn period and act to increase vascular permeability and induce tissue damage. The vasodilator prostaglandin E_2 is found in the kidneys and counteracts the effect of many vasoconstrictors. Its production, however, is inhibited in the early phases of burns and when sepsis develops.[5,7,10,12]

Circulating mediators that originate from the burn wound, such as interleukin 6, interleukin 8, and tumor necrosis factor, contribute to the hypermetabolic and inflammatory response in burned patients.[13,14] Although in this study these mediators were not examined, it is proposed that they interfere with elevated levels of stress-related hormones and promote prolonged vasoconstriction with a potential higher risk of acute renal failure.[13,14] Early wound excision and grafting may decrease the inflammatory response and thus improve renal blood flow and decrease the severity of renal failure. In this study, the time delay from burn injury to the first excision and grafting was reduced by 83% in the period from 1984 to 1997 when compared with the period from 1966 to 1983. Furthermore, there were significant differences ($P<.05$) in excision and grafting delays between those patients who received or did not receive dialysis. The patients who did not require dialysis had wound excision performed significantly earlier compared with those receiving dialysis, indicating that early wound excision is associated with a better outcome in patients with renal failure. When children with acute renal failure who survived were compared with those who did not survive, however, there was no significant difference ($P=.2$).

As we have shown, acute renal failure occurs either immediately after the burn injury or after 2 weeks. The later form of acute renal failure is often associated with sepsis.[10] The incidence of sepsis dropped significantly from 71% in the former study group to 44% in the more recent study group. A similar decrease in the incidence of sepsis could also be found by comparing survivors with acute renal failure with nonsurvivors with acute renal fail-

ure from 1984 to 1997. Whereas the incidence of sepsis was 60% in those who did not survive, it was 19% in those who survived. A similar pattern could be found by comparing burned children requiring dialysis with those not requiring dialysis. Twelve (60%) of 20 children who required dialysis treatment had sepsis, whereas 6 (38%) of 16 children who did not require dialysis had sepsis. These data indicate that a change in infection control, including a change in antibiotic therapy, early wound excision, better wound coverage, and improved critical care, decreased the incidence of sepsis in the recent time and thus may have improved the survival outcome in children with acute renal failure.

Early acute renal failure is mainly associated with hemodynamic disorders in the kidneys[7,8]; thus, early fluid resuscitation should lessen the severity of acute renal failure. In this study, from 1966 to 1983, the mean time between burn injury and the initiation of intravenous fluid resuscitation was approximately 9 hours. The mean time between burn injury and the initiation of fluid resuscitation decreased to 3 hours after 1983. Furthermore, by comparing survivors vs nonsurvivors in the group from 1984 to 1997, survivors had a resuscitation delay of less than 2 hours whereas nonsurvivors had a resuscitation delay of nearly 5 hours. We showed that the mean time between a burn injury and the initiation of fluid resuscitation decreased from a mean of 15 hours from 1966 to 1975 to a mean of 5 hours from 1976 to 1983; no significant improvement in survival outcome could be shown, however. It was only when the mean time between a burn injury and beginning adequate intravenous fluid resuscitation was less than 2 hours that a significant improvement in the survival rate in patients with acute renal failure could be found (Figure 3). In addition, a comparison with patients requiring dialysis and those not requiring dialysis showed that there was a 5-hour delay in starting the fluid resuscitation in those receiving dialysis compared with a 2-hour delay for those not receiving dialysis. Thus, it appears that early fluid replacement moderates kidney damage, prevents the severe manifestations of acute renal failure, and thus improves the survival outcome.

In this study, 6 (38%) of 16 patients who required dialysis survived, and none of these required long-term dialysis treatment after discharge from the hospital. In patients with other critical illnesses, the use of dialysis for acute renal failure has not been shown to affect survival.[14] We showed a similar result, as we could find no difference in the use of dialysis between the 2 periods, but with the change in therapies around 1984, overall mortality improved. In fact, those requiring dialysis in the more recent group had a longer resuscitation delay, increased times to wound excision, and a higher incidence of sepsis, perhaps being associated with a greater severity of renal injury. Despite this, 6 (38%) of 16 patients who required dialysis survived, although the efficacy of dialysis was not shown.

With improved resuscitation time, better infection control, and early wound excision, it appears that the severity of insult is reduced. Evidence to support this is that the incidence of acute renal failure between the periods did not change, but survival in patients with acute renal failure did. In this study, we did not examine the severity of renal injury in relation to the above variables. Mortality rates from 1984 to 1997 in burned children in whom acute renal failure developed are similar to recent data published on adult burned patients with acute renal failure.[15,16] From our data, we can conclude that the improvement in mortality rates in burned children with or without acute renal failure was due to modifications in the therapeutic approach to burn care. Comparing the mortality in burned children with acute renal failure from 1966 to 1983 with those with acute renal failure from January 1984 to January 1997, the mortality decreased from 100% to 56%. In the same period, a decrease in mortality occurred from 33% to 14% in burned children without acute renal failure. Changes that have influenced this improvement include early wound excision, better infection control, and early fluid resuscitation.

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