

## BRIEF CLINICAL REVIEW

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# Acute Kidney Injury and CRRT in Burn Patients

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Acute Kidney Injury (AKI) is a common complication in burn patients. In one study involving 60 patients with Total Body Surface Area (TBSA) burns of 20% or more, AKI (defined by RIFLE category) occurred in 53% of patients. AKI in burn patients is associated with higher mortality, increased length of mechanical ventilation, and ICU stay. It also has long-term consequences including increased risk of chronic kidney disease, conversion to chronic dialysis, hospital readmission and long-term mortality.<sup>1</sup> The application of renal replacement therapy (RRT) may be helpful in the management of acute renal failure in these patients with a uniquely complex fluid balance and inflammatory physiology.

Renal impairment in burn patients is related to the combined insults of massive fluid shifts, release of inflammatory cytokines and hormone mediators, myocardial depression, and toxic drug exposures.<sup>2</sup> A study by Palmieri et al,<sup>3</sup> reported that progression of AKI in burn patients did not correlate with age or severity of illness at the time of admission but to other factors such as presence of sepsis, use of nephrotoxic agents, cumulative fluid balance and number of surgeries before progression of AKI. The authors suggested that manipulations of burn wounds during surgeries cause a release of inflammatory mediators as well as transient bacteremia that can adversely affect renal function.<sup>4</sup> In addition, aggressive intravascular fluid replacement and positive fluid balance may increase intra-abdominal pressure, resulting in decreased renal flow in critically ill patients.<sup>5</sup>

Renal injury, when seen within the first few days of the burn injury, is related to massive fluid shifts, with intravascular hypovolemia, low cardiac output and systemic vasoconstriction.<sup>6</sup> Hauben<sup>7</sup> reported that the volume of circulating plasma is reduced by 25% of the normal value with burns involving more than 40% TBSA. However, this is now less common due to aggressive volume resuscitation during the acute stage of burn management. The second form of renal injury develops during the second week and is related to sepsis and multi-organ failure. This is now believed to be the most frequent cause of renal insufficiency in burn patients.<sup>6</sup>

The management of acute renal failure (ARF) in burn patients is usually supportive care with or without a consulting nephrologist. The use of renal replacement

therapy (RRT) in burn patients with ARF remains low and the usual indications include fluid overload, hyperkalemia, pulmonary edema, diuretic failure, severe acidosis and uremic complications. The optimal time to initiate RRT in critically ill patients with ARF is not known, and there is a wide variability when RRT is initiated in ICU. Continuous Renal Replacement Therapy (CRRT), as compared to single-pass hemodialysis, seems to be the preferred mode of renal replacement therapy for critically ill burn patients with AKI, since these patients are usually hemodynamically unstable, mechanically ventilated and septic. CRRT allows for a negative fluid balance without significant hemodynamic shifts<sup>8</sup> and is associated with extra renal benefits such as reversal of shock, improvement of ARDS and decreased neurohumoral activation.<sup>9</sup> In a 2009 retrospective cohort study published by Chung and colleagues,<sup>10</sup> the application of CVVH in adult patients with greater than 40% TSBA burns and AKI, defined as Acute Kidney Injury Network (AKIN) stage 3 or AKIN stage 2 with shock, was associated with reduced hospital mortality when compared with historical controls that did not receive any form of renal replacement. In addition, the authors noted a dramatic reduction in the vasopressor requirement and need for supplemental oxygen at 24 hours. Liew and colleagues published a descriptive analysis of a series of burn patients admitted to Singapore General Hospital that were prescribed early RRT for AKI. Indications for dialysis included serum creatinine > 1.5 times baseline or UOP < 0.5 ml/kg/h for at least 2 consecutive hours. Matched historical controls were used for comparison. The authors concluded their study supported early use of RRT, with a mortality rate in early RRT group of 37% as compared to 66.7 % in the control group.<sup>11</sup>

In non-burn patients with severe sepsis, there are mixed results regarding the efficacy of RRT. The positive studies suggest that early application of RRT can be beneficial, as it can modify the plasma concentrations of inflammatory mediators.<sup>12</sup> There are also no clear guidelines as to the precise timing for initiating RRT. A joint statement by leading pulmonary and critical care societies in 2010<sup>13</sup> proposed that RRT should not be delayed in critically ill patients with AKI and metabolic derangements simply because of persistent urine production. This is supported by the single-center ELAIN trial which showed that early RRT, initiated at KDIGO stage 2, significantly reduced all-cause

mortality at 90 days as compared to delayed RRT initiation.<sup>14</sup> However, a multicenter randomized trial published by Gaudry and colleagues,<sup>15</sup> randomized patients to receive early (n=311) versus delayed RRT for KDIGO stage 3 disease (n= 308) and found no difference in mortality (48.5% vs 49.7%; P=0.79). There was a significant increase in catheter related blood stream infection in the early RRT group. Additionally, 49% of patients within the delayed RRT group never received RRT. The contrasting results between the two trials could be related to different study designs and different thresholds for initiating RRT, and demonstrate the conflicting data surrounding RRT in critically ill patients.

The level of evidence guiding initiation of RRT as well as the timing of RRT in critically ill patients remains weak. This is especially true among critically ill burn patients where the studies are retrospective, observational cohort studies and small underpowered prospective trials. However, the available evidence seems to point towards improved survival in burn patients with CRRT,<sup>16</sup> providing the rationale for expert consensus that advocates for 'early' initiation of RRT in critically ill patients before the development of extreme metabolic derangements. However, additional prospective randomized studies are required before this becomes a standard of care.

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