Continuous Venovenous Hemofiltration to Reduce Mortality in Severely Burned Patients

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9.1 General Principles

Among severely burned patients who require hospitalization, the prevalence of acute kidney injury (AKI) has been reported to be close to 25 %, with an associated mortality of 35 % [1]. Among those who require renal replacement therapy (RRT), the reported mortality is up to 80 %, and it is likely higher than in the non-burn critically ill population (60 %) [1, 2]. It is presumable that this high associated mortality is closely tied to burn size and age and thus relatively non-modifiable. However, recent studies suggest that it is possible to alter survival in this patient population with an early, aggressive approach to RRT. More importantly, the traditional approach of waiting for classically taught triggers for the initiation of RRT (such as refractory acidosis, severe electrolyte abnormalities, intoxication with dialyzable substances, intractable fluid overload, and uremic complications such as pericarditis and encephalopathy) may result in an unacceptably high mortality [3].

The specific mode of RRT also deserves careful consideration for the treatment of AKI in burned patients. Convective solute clearance through hemofiltration-based RRT has theoretical advantages in the setting of an augmented immune/inflammatory state, due to the nonspecific removal of middle molecular weight mediators (10–50 kDa) [4]. In contrast, solute diffusion with reliance on concentration gradients through hemodialysis-based RRT only effectively targets small molecules. The contrast between continuous and intermittent modes of RRT and their corresponding clinical implications is also of interest in the burn population. It is commonly accepted that continuous modes are better tolerated from a hemodynamic standpoint than intermittent therapies [5, 6]. Additionally, continuous therapies may be associated with better long-term outcomes as defined by less need for long-term dialysis among survivors [7, 8].

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G. Landoni et al. (eds.), *Reducing Mortality in Acute Kidney Injury*,
DOI 10.1007/978-3-319-33429-5_9

Therefore, a reasonable argument can be made for continuous venovenous hemofiltration (CVVH) as the mode of choice for severe burns with AKI. A recent systematic review revealed only one study suggesting that this intervention improves mortality [9]. This study and its implications will be reviewed in this chapter.

9.2 Main Evidence

Early reported experience in burns by Leblanc et al. [10] suggested that continuous renal replacement therapy (CRRT) was hemodynamically well tolerated while providing good metabolic and volume control. Their reported mortality rate was however 82 %, similarly to other reports, which also showed high mortality rates among burn patients treated with CRRT [11–14].

In a study comparing early aggressive CRRT in burned military casualties, a decreased in-hospital mortality from 88 % to 56 % was demonstrated when comparing a treated group to a historical control of patients who were managed using the conservative approach of waiting for traditional dialysis indications [14]. Of note, none of the patients in the conservative arm survived long enough to meet the criteria for dialysis, and thus, none were offered any form of RRT. When the sample size was nearly doubled with the addition of civilian burn patients treated in the same facility, the improvement in survival was sustained [15]. Again, only a small fraction of patients in the conservative arm (2/28) received any form of RRT, suggesting that applying traditional dialysis initiation criteria in burns only leads to an unacceptably high death rate. Interestingly, a significant improvement in hemodynamic parameters was observed among those who were placed on CVVH while in shock ($n=21$), with most of them being completely weaned off vasopressor support within 48 h. Additionally, patients with acute respiratory distress syndrome (ARDS) had a significant improvement in oxygenation within 24 h from CVVH initiation ($n=16$).

This study certainly has some limitations: the sample size is small, the study is retrospective and it is from a single center. Therefore, caution should be applied when interpreting these findings into actual practice. Accordingly, the first web-enabled international consensus conference on mortality reduction in patients with or at risk for AKI recently recommended against the routine application of CVVH in severely burned patients with the intent of increasing survival [9]. Nonetheless, it is important to individualize interventions based on the best available evidence when dealing with a niche population such as burns, where robust populations do not readily exist for the purposes of large randomized multicenter studies. In fact, if on the one hand the impact of this specific therapy on survival in burn patients with AKI is probably unclear, on the other hand, an unacceptably high mortality is almost certain if no therapy is applied in this setting.

9.3 Pathophysiological Principles

Treatment of burn patients with CVVH resulted in an observed improvement in hemodynamics and lung function [15]. This suggests a potential extrarenal benefit. Hemodynamic improvement has been observed in other studies where a relatively high dose of replacement volumes has been used [16]. In the discussed study on CVVH in burned patients, the mean hemofiltration dose prescribed was 57 ± 19 mL kg^{-1} h^{-1} [15]. This dosage places this technique in the "high-volume hemofiltration" category, capable of removing circulating mediators and cytokines from the blood compartment, as demonstrated in numerous preclinical studies [16]. The profoundly dysregulated inflammatory host response observed in the critically ill burn population may thus be ideally suited for this type of approach [17]. Regardless, it is not possible to attribute any potential benefit to an aggressively applied (high-volume) mode of therapy (hemofiltration) in the right population (burns) as early application (timing) may also be a factor.

High-volume hemofiltration (70 mL kg^{-1} h^{-1}) applied in a critically ill population was not found to be superior to a lower dose of hemofiltration (35 mL kg^{-1} h^{-1}) in a randomized controlled trial [18]. Caution should be applied in the extrapolation of these findings to the burn population.

Obviously, more carefully designed studies are needed. However, while the optimal mode and dose of therapy in burns continue to be up for debate, it is clear that waiting for "traditional" dialysis indications only leads to an unacceptably high mortality rate in this unique population. Early and aggressive application of some form of RRT regardless of mode and dose may be better than waiting for arbitrary and absolute triggers.

9.4 Therapeutic Use

Application of CVVH, especially higher doses, comes with some unique practical considerations. Some of these have been mentioned in the Clinical Summary. First, as with any mode of RRT, regular monitoring of electrolytes is a must. In particular, given that the convective approach can remove larger molecules in the middle molecular weight range, extra attention should be paid to avoidance of hypophosphatemia. Second, the mode and dose of therapy, along with native renal clearance, need to be taken into account when determining appropriate doses of therapeutic drugs such as antimicrobials [19]. Finally, when applying a higher hemofiltration dose by increasing the replacement fluid rate, careful consideration of the filtration fraction is needed, and blood flow must be increased accordingly to avoid early clogging of the filter [20]. In general, a filtration fraction less than 25 % is desired to maintain adequate filter patency. This can be achieved by increasing the blood flow rate of the circuit along with the replacement fluid rate.

Clinical Summary

Technique	Indications	Cautions	Side effects	Dose	Notes
CVVH	AKI in burns	Dose adjustment of antimicrobials needed	Electrolyte depletion Loss of micronutrients	20–35 mL kg^{-1} h^{-1}	Early initiation may be beneficial
High-volume hemofiltration	AKI in burns with septic shock	Dose adjustment of antimicrobials needed	Electrolyte depletion Loss of micronutrients	>35 mL kg^{-1} h^{-1}	Evidence in the general critically ill population suggests no benefit Appears to be safe

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