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# Continuous vs. intermittent hemodialysis: With which spin will my patient win?

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## Expanded Abstract

### Citation

Vinsonneau C, Camus C, Combes A, et al. Continuous venovenous haemodiafiltration versus intermittent haemodialysis for acute renal failure in patients with multiple-organ dysfunction syndrome: a multicentre randomised trial. Lancet 2006;368(9533):379-85 [1].

### Background

Whether continuous renal replacement therapy is better than intermittent haemodialysis for the treatment of acute renal failure in critically ill patients is controversial.

### Methods

**Objective:** To compare the effect of intermittent haemodialysis and continuous venovenous haemodiafiltration on survival rates in critically ill patients with acute renal failure as part of multiple-organ dysfunction syndrome.

**Design:** Prospective, randomized, controlled trial

**Setting:** 21 medical or multidisciplinary intensive-care units from university or community hospitals in France between Oct 1, 1999 and March 3, 2003.

**Subjects:** 360 critically ill patients with acute renal failure as part of multiple-organ dysfunction syndrome.

**Intervention:** Patients were randomized to intermittent haemodialysis (n=184) or continuous venovenous haemodiafiltration (n=175). Guidelines were provided to achieve optimum haemodynamic tolerance and effectiveness of solute removal in both groups. The two groups were treated with the same polymer membrane and bicarbonate-based buffer.

**Measurements and main results:** The primary endpoint was 60-day survival based on an intention-to-treat analysis. Rate of survival at 60-days did not differ between the groups (32% in the intermittent haemodialysis group versus 33% in the continuous renal replacement therapy group [95 % CI -8.8 to 11.1,]), or at any other time.

### Conclusion

These data suggest that, provided strict guidelines to improve tolerance and metabolic control are used, almost all patients with acute renal failure as part of multiple-organ dysfunction syndrome can be treated with intermittent haemodialysis.

## Commentary

Acute renal failure occurs frequently in critically ill patients and is associated with mortality as high as 60% [2]. The goal of renal replacement therapy is to achieve adequate correction of uremia, electrolyte abnormalities, and volume overload while ensuring good hemodynamic tolerance. Since it was first described in 1977, continuous renal replacement therapy (CRRT) has become an increasingly popular alternative to intermittent hemodialysis (IHD) in critically ill patients. The theoretical advantages of CRRT are increased time-averaged dialysis dose, less hemodynamic instability, and, possibly, removal of high molecular weight solutes, such as inflammatory cytokines [3].

Despite its potential clinical advantages, CRRT has not been shown to be superior to IHD. Several studies compared CRRT to IHD using retrospective observational designs, with inherent differences between treatment groups, such as type of dialysis membrane used and baseline illness severity, limiting the usefulness of their findings. Three prospective randomized trials have

compared CRRT to IHD. One study suggested that CRRT increased mortality [4], though imbalanced randomization biased the study against CRRT. After adjusting for disproportionally distributed covariates, mortality did not differ between groups. The other two randomized studies failed to show a difference for mortality or other endpoints, but were small and underpowered [5,6].

The current study by Vinsonneau and colleagues is the latest attempt at determining which modality is superior. A heterogeneous group of 360 medical and surgical ICU patients with acute renal failure as part of the multiple organ dysfunction syndrome (MODS) were randomized to CRRT (specifically, continuous venovenous hemodiafiltration) versus IHD in 21 ICUs throughout France. At study entry, nearly all subjects were mechanically ventilated, almost 90% were on vasopressors, and more than half had sepsis. Guidelines were provided to achieve optimum metabolic control and hemodynamic stability. For CRRT, this included a blood flow of 120 mL/min or more with the objective to maintain urea concentration at less than 30 mmol/L. For IHD, the recommendation was to keep a blood flow of 250 mL/min or more with the objective of a urea reduction ratio greater than 65% for each session. The study used the same membranes in each group and there was no measurement of the delivered dialysis dose once treatment was initiated. The authors found that there was no difference in mortality, ICU or hospital length of stay, or rate and time to renal recovery. There were no differences in adverse event rates, such as hypotension or thrombocytopenia, though the CRRT group did develop hypothermia more frequently (17% vs. 5%, p=0.0005). The authors concluded that, provided strict guidelines to improve tolerance and metabolic control, almost all patients with acute renal failure as part of MODS can be treated with IHD.

This was a well-conducted study with successful randomization ensuring balance in clinically important patient characteristics at baseline. A few limitations, however, deserve consideration. The study was relatively small and only powered to detect a 15% absolute difference in 60-day mortality. With a 1.1% absolute difference in mortality rates, it is difficult to imagine there is a clinically meaningful difference in outcome between groups. Proving statistical significance would have required a study two orders of magnitude larger in size. The “dose” of therapy was not specified in either group. The average delivered dose in the CRRT group (29 mL/kg/hr) was below the dose shown to improve survival (35mL/kg/hr) in the one recent study [7]. There was no assessment of the delivered dose in the IHD group once treatment was started. Thus, the delivered dose in both arms might have been suboptimal. Additionally, there is a lack of information about subsequent co-interventions, such as vasopressor and fluid therapy, which could have been used differentially between groups in this non-blinded study and, therefore, influenced mortality. Finally, there is a curious finding that the mortality rate in the IHD group decreased significantly overtime, whereas mortality in the CRRT group remained stable. Though changes in the dialysis membrane were made by the manufacturer mid-study [8], these did not appear to have any effect on mortality. Nor could the change in survival be explained by changes in case-mix or a center-specific effect. The authors raise the possibility that standard of care improvements during the study could have favored IHD, but found no evidence of such an effect in an analysis of a similar patient population treated with IHD in France during the same period [9].

## Recommendation

Based on the results of this study, is appears that virtually all critically ill patients with acute renal failure and MODS can be treated with intermittent hemodialysis if appropriate attention is paid to hemodynamic and metabolic control. Questions such as whether a specific patient will do better with a particular modality or the optimal time to switch from one method to the other are unanswered by this study and may depend, at least in part, upon the level of expertise of a particular center with each modality.

## Competing interests

The authors declare no competing interests.

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