

IMPROVING SURVIVAL WITH A GREATER DIALYSIS DOSE IN PATIENTS WITH AKI: DOES IT DEPEND ON EARLY ONSET OF TREATMENT?

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Introduction: Conflicting results have been reported concerning dialysis dose in continuous renal replacement therapy (CRRT) during acute kidney injury (AKI). The influence of a greater dose (40ml/kg/h) compared to a standard dose (20ml/kg/h) on survival in critically ill patients is still under the scope as well as the addition of diffusion (CVVHDF) to convection (CVVH). We studied the hypothesis that timing of treatment initiation may play a role in survival in this population and explain different results between the few studies done so far.

Material and methods: In a previous trial (Saudan et al. *Kidney Int* 2006), we randomised patients to receive either continuous venovenous hemofiltration (CVVH with 1-2.5l/h replacement fluid) or continuous venovenous hemodiafiltration (CVVHDF with 1-2.5l/h replacement fluid + 1-1.5l/h dialysate) according to their body weight and analysed their survival at 90 days. Patient were eligible for renal replacement therapy if they fulfilled the inclusion criteria of oliguria (urine output < 200ml/12h) despite fluid resuscitation and intravenous diuretics and/or azotemia (urea > 30mmol/l). Exclusion criteria were: reversible prerenal failure or postrenal failure, suspicion of glomerular disease, end stage renal failure and patients on ACE inhibitors.

In the present study we compared patients requiring renal replacement therapy within and after the first 48 hours of intensive care unit (ICU) admission to understand the role of this timing on survival. Kaplan Meier curves and cox regression were made using variables that were significant in univariate analysis (p < 0.05) or known to be important on survival in ICU patients.

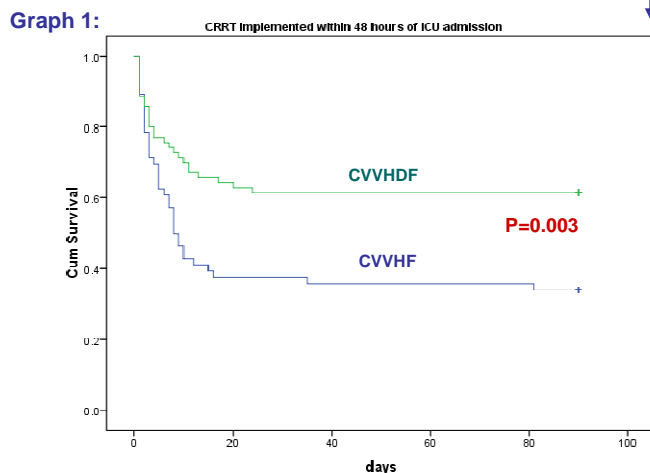
Results: We randomised 206 patients from October 2000 to December 2003. From this population, 126 patients were treated within the first 48 hours of ICU admission (early treatment) and 80 after 48 hours (late treatment). Demographics and clinical characteristics are shown in **table 1**.

Table 1: Patients characteristics at baseline according to treatment time

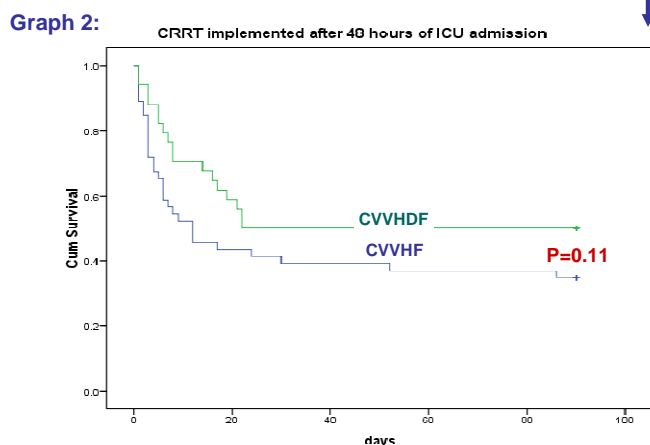
Variables	Early treatment (n=126)	Late treatment (n=80)	p
Age (years)	63.2 ± 14.7	63.0 ± 12.7	0.93
Male / Female	76/50	50/30	0.75
Weight (kg)	72.3 ± 16.6	74.3 ± 19.0	0.44
Diabetes (%)	27 (21.4)	15 (18.8)	0.64
Sepsis (%)	77 (61.1)	49 (61.3)	0.98
APACHE II score	25.3 ± 9.8	24.4 ± 8.9	0.53
SOFA score	9.6 ± 5.3	10.1 ± 4.9	0.48
Diagnosis of renal failure (surgical/trauma/medical)	22/7/97	25/8/47	0.021
Urea (mmol/l)	28.5 ± 14.7	31.4 ± 12.3	0.15
Creatinine (µmol/l)	464.6 ± 296.9	371.2 ± 169.6	0.005
Time from ICU admission to CRRT (days)	0.69 ± 0.76	9.0 ± 8.9	<0.001
Duration of mechanical ventilation (days)	5.1 ± 7	12.6 ± 11.3	<0.001
Duration of hospital stay (days)	34.9 ± 39.7	58.5 ± 66.0	0.005
Randomisation: CVVH / CVVHDF	56/70	46/34	0.68

Both groups were similar in terms of treatment randomisation (CVVHDF vs CVVH), age, gender, severity scores (APACHE, SOFA), baseline urea levels and prevalence of sepsis and diabetes. However patients starting renal replacement therapy later had mostly a medical diagnosis, stayed longer in hospital, needed longer ventilation and had lower levels of creatinine.

In **graphics 1 and 2**, we analysed 90-day survival according to time therapy delay and treatment randomisation. Among those treated within 48 hours of ICU admission (**graph 1**), the CVVHDF group (n=70) had a significantly higher 90-day survival of 61% compared to 34% in the CVVH group (n=56).



Among those treated after 48 hours of ICU admission, 90 day survival was 50% for the CVVHDF group (n=34) and 35% for the CVVH group (n=46). This difference was not significant.



We analysed factors predicting 90-day survival using a Cox multivariate analysis model (**table 2**).

After insertion of time from ICU admission to CRRT initiation in the model, randomisation to CVVHDF remained however an independent predictor factor for survival. Age, APACHE II score and BUN at initiation of therapy were others predictors.

Table 2: Results of Cox's proportional hazards models (90-days survival)

	Hazard ratio	95% CI	p
Age	1.02	1.01-1.04	0.06
Gender (female=1)	0.726	0.46-1.14	0.16
Weight	0.998	0.99-1.01	0.70
Sepsis	0.76	0.49-1.17	0.21
APACHE II score	1.06	1.03-1.08	<0.00
Diagnosis:			
surgical			0.25
trauma	1.68	0.74-3.83	0.22
medical	1.49	0.89-2.49	0.22
Urea	0.98	0.96-0.99	<0.01
Time from ICU admission to CRRT	1.02	0.99-1.04	0.17
Randomisation: CVVHDF	0.59	0.40-0.88	0.01

Conclusions: The results of our study suggest that in patients with AKI needing CRRT a higher dialysis dose may confer a better survival when therapy is initiated within the first 48 hours of ICU admission. Discrepancies between trials studying the effect of dialysis dose could be explained by a different timing in CRRT implementation.