

Commentary

Dose of dialysis in the intensive care unit: is the venom in the dose or in the clinical experience?

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See related research by Vesconi *et al.*, <http://ccforum.com/content/13/2/R57>

Abstract

Many studies on the most 'adequate' dose of renal replacement therapy (RRT) in critically ill patients with acute kidney injury have obtained contradictory results. The previous issue of *Critical Care* reports a multi-centre study showing that a higher than conventional dose of RRT, whether continuous RRT or intermittent RRT, is not associated with better survival of these patients. This commentary highlights some of the problems associated with the interpretation of this and previously published studies. These problems include the use of targets of Kt/V urea or the ultrafiltration rate in millilitres per kilogram body weight, the latter quite difficult to estimate in these patients, the divergent co-morbidities of the patients, and the local experience of intensivists or nephrologists with either continuous RRT or intermittent RRT. The last factor could explain why some single centre studies did find an impact of dialysis dose on the survival of these patients whereas multi-centre studies did not.

In the previous issue of *Critical Care*, an article by Vesconi and colleagues [1] describes the impact of the dose of renal replacement therapy (RRT) on clinical outcomes in critically ill patients with acute kidney injury. This study was performed in a number of European intensive care units (ICUs). Dialysis dose was defined as more intensive (continuous RRT (CRRT), >35 ml/kg/h; intermittent RRT (IRRT), >6 sessions/week) or less intensive (CRRT, <35 ml/kg/h; IRRT, <6 sessions/week). The study did not provide evidence for a survival benefit of a higher dose of RRT. However, more intensive RRT was associated with a favourable effect on ICU stay and duration of mechanical ventilation among the surviving patients. Studies of this nature are not easy to perform and the authors are to be commended for their initiative.

This paper highlights many of the controversial aspects of RRT management in these patients, including when to start, which modality is preferable, and what dose to apply. These controversies are partly fuelled by a lack of consistent data,

which are difficult to obtain in this heterogeneous patient group, with wide ranges of applied practices and underlying diseases and the absence of universally accepted definitions.

For example, analysis of Table 1 in the paper by Vesconi and colleagues [1] reveals the wide diversity of the patient study population involved; the distribution of the RIFLE classification at the start of RRT is intriguing as a substantial portion of the patients was started on dialysis without even having class 'I' of RIFLE. Besides the fact that the RIFLE criteria are not intended to be a guide as to when to start RRT, this means that some of these patients had near 'normal' serum creatinine levels at the beginning of RRT. The question can be raised as to whether the inclusion of such patients influenced the outcome, although it is unclear how and to what extent this might be the case.

Another question to be considered is how the results of this study should be interpreted in the context of other dose of dialysis/outcome randomized trials using CRRT (continuous haemofiltration or haemodiafiltration), IRRT - including the conventional 3 to 4 hour sessions or the prolonged slow extended dialysis (SLED) method - or both. Obviously, such studies produced mixed results. Some showed a benefit of the 'higher than usual doses' [2-4], but others did not [5-8]. All these studies were accompanied by a number of critical reviews and editorial comments [9-12]. Although none of the studies showing no benefit of higher dose of RRT were perfect, all have one advantage: they reflect daily practice. This is also the conclusion of the paper by Vesconi and colleagues. Does this mean that dialysis dose is not important? Probably not. The problem is that we have no correct understanding of what 'dose' means and higher doses implicitly mean more complications and/or comorbidities.

CRRT = continuous RRT; ICU = intensive care unit; IRRT = intermittent RRT; RRT = renal replacement therapy.

In the study by Vesconi and colleagues, differences in dose for CRRT were not pursued intentionally but seem to have been the consequence of external conditions, of which body weight of the patients was the main one. The patients with the lowest dose of CRRT were approximately 33% heavier than those with the highest dose. This is, of course, an important and remarkable confounder. In interventional studies where dialysis dose is normalized to body weight, other difficulties may arise as well. What should be considered as 'body weight': dry weight, weight before admission, real *ad hoc* weight, distribution volume of urea, or something else? And how do we estimate this sometimes quite fluctuating 'body weight' in a critically ill patient? In the IRRT group, the dose was expressed as the number of dialysis days per week, targeting a Kt/V urea threshold. However, as long as we know neither the nature nor the kinetics of many of the 'toxins' involved in the acute 'uraemic syndrome' we will always have to rely on surrogate markers, of which the volume status of the patient - which should be frequently clinically evaluated - and electrolyte and acid-base disturbances - which should be managed - are probably the most important. As such, the fact that absolute ultrafiltered volumes were comparable in both the less and more intensive patient groups makes it questionable whether there really was a difference of dose in the study by Vesconi and colleagues. Interestingly, there was also no difference in obtained net ultrafiltration between low and intensive dose groups in the VA/NIH trial [7] and a study by Tolwani and colleagues [8]. So, maybe our 'concept' of what dose actually means in ICU patients needs to be redefined.

Another problem of 'dose' is that it comes at a price. The high dose group in the VA/NIH study [7] suffered a substantially higher number of complications, such as haemodynamic instability and electrolyte disturbances. The potential benefit of achieving more clearance can thus be eliminated by a higher complication rate. Complication rates might, in turn, be corrected by centre experience; this could explain why the first, but single centre, study of Ronco and colleagues [2] found that dialysis dose did have an impact whereas the multicentre VA/NIH study [7] did not. As the latter study enrolled approximately 500 patients in 30 centres, it can be presumed that a substantial number of the study centres recruited less than 10 patients per year. The 'dose of experience' with RRT in the ICU might be a greater determining factor of outcome in critically ill acute kidney injury patients than the dose of dialysis.

Finally, despite the previous seminal study [2] by the senior author of the paper by Vesconi and colleagues demonstrating that a 'high' dose of 35 ml/kg/h CRRT is advantageous, the latter study shows that, in daily clinical practice, this dose is quite difficult to achieve. It should be appreciated by readers that the same advocates of a high dose of RRT are now amending their previous recommendations.

Competing interests

The authors declare that they have no competing interests.

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