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# Renal Replacement II: Dialysis Dose

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Acute renal failure (ARF) often develops in the setting of other organ dysfunction in critically ill patients. ARF has a significant impact on patient morbidity and mortality [1–5]. Current management of ARF includes optimization of hemodynamic and volume status, avoidance of further renal insults, optimization of nutrition, and institution of renal replacement therapy (RRT). Indications for RRT include oligoanuria, decreased creatinine clearance, severe acidemia, hyperkalemia, and other metabolic and electrolyte disorders linked to kidney failure. It is recognized that morbidity and mortality are strictly correlated to hemodialysis (HD) dose in patients who have end-stage renal disease (ESRD) [6–9], and current practice guidelines recommend a minimum standard treatment dose [10]. Nevertheless, the Hemodyalysis study, examining the effect of intermittent hemodialysis (IHD) dose, failed to confirm the intuition that "more dialysis is better" [11]. Optimal strategies to improve patient morbidity and mortality in ARF have not been examined in such a clinical trial. However, some authors have suggested recently that improved survival of critically ill ARF patients could be correlated to delivered therapy dose [12–18]. This article focuses on RRT dose measurement and prescription in the intensive care setting as well as the current scientific evidence concerning RRT dose and outcome.

## Dose measurements in acute renal replacement therapy

The treatment dose of RRT can be defined by various aspects such as efficiency, intensity, frequency, and clinical efficacy. Efficiency of RRT can be

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represented by clearance (K). Technically, K depends on blood flow rate, dialysate flow rate, ultrafiltration rate, reference molecules, and hemodialyzer type and size. K can be normally used to compare the treatment dose within each modality. Between different modalities, however, K is typically higher in IHD than continuous renal replacement therapy (CRRT) and sustained low efficiency dialysis, even though IHD does not remove the solutes better than the others. This is not surprising, because K represents only the amount of treatment per unit of time. Therefore, K cannot be employed to compare various modalities differing in treatment duration. Finally, K represents an instantaneous measurement, and it correlates with the amount of solute removal at the time point of the measurement. Although K might remain stable over time, if blood levels of the reference molecule will change, removal rate will also change. Intensity of RRT can be described by the product of clearance × time (Kt). Because the time is accounted, Kt is more effective than K in the comparison of various RRT modalities. Frequency is an essential factor to further describe treatment dose in different modalities. Thus weekly clearance, intensity × frequency (Kt × treatment d/wk), is superior to Kt because it offers the comparison of different modalities in the more extensive view. Clinical efficacy of RRT represents the effective clinical outcome resulting from the implication of a given treatment. It can be described by a fractional clearance (Kt/V) where V is the volume of distribution of the marker molecule. Kt/V is an established maker of adequacy correlating with survival in chronic hemodialysis patients [19]. Hence, Kt/V is widely applied clinically in patients with ESRD, but its application in patients with ARF requiring emergent dialysis has not been rigorously validated.

The search for specific toxins to be cleared, furthermore, has not been successful despite years of research, and urea and creatinine are generally used as ''marker'' solutes to measure renal replacement clearance for renal failure. Although available evidence does not allow direct correlation of the degree of uremia with outcome, in the absence of a specific solute, clearances of urea and creatinine are used in chronic renal disease to guide treatment dose, and a single-pool $Kt/V_{UREA}$ of at least 1.2 is currently recommended [10].

Kt/V application on treatment dose in the acute setting is theoretically intriguing, but many concerns have been raised by its practical use. Problems intrinsic to ARF can hinder the accuracy of dose measurement; these include the lack of a steady state, uncertainty about urea volume of distribution ($V_{UREA}$), high protein catabolic rate, labile fluid volumes, and eventual residual renal function. Furthermore, delivery of a prescribed dose can be limited by technical problems such as access recirculation, poor blood flows with temporary venous catheters, clotting, and mechanical inaccuracies; clinical issues such as hypotension and vasopressor requirements can be responsible for solute disequilibrium within tissues and organs.

Time-averaged blood urea nitrogen ($TAC_{UREA}$) is the area under the sawtooth curve produced by intermittent dialysis sessions. $TAC_{UREA}$ is a function of dialysis dose, but it is also associated with urea generation rate (G) and protein intake with nutrition. As such, it is not a good indicator of RRT dose.