In Focus

Do we need another $K_t/V$?

James Tattersall
Renal Medicine, Leeds Teaching Hospitals Trust, Leeds, UK

Correspondence and offprint requests to:
James Tattersall;
E-mail: jamestattersall@nhs.net

A new method of estimating $K_t/V$ has been proposed. This was a required update to accommodate frequencies of dialysis other than thrice weekly [1]. The original approximate method for calculating $K_t/V$ from pre- and post-dialysis urea concentrations was developed using linear regression on a data set of measurements taken from patients undergoing thrice-weekly dialysis. The method assumes that the interval between the blood samples and preceding dialysis was 2 days. Unfortunately, when dialysis is delivered other than over a standard thrice-weekly schedule, the existing approximate method for $K_t/V$ becomes inaccurate. A different correction factor for the urea generation rate is required, taking the frequency and duration of the preceding interdialytic interval into account.

There are now at least 11 different ways of quantifying small-solute clearance in dialysis (Table 1), 7 of which are different kinds of $K_t/V$. In addition, there are at least five different approximation methods for calculating $K_t/V$ (Table 2).

$K_t/V$ was initially used to quantify the dose of a single haemodialysis (HD) session in terms of urea clearance ($K$) and time ($t$) [2]. $K_t/V$ is the exponential term describing the changing urea concentration during the dialysis session. $K_t/V$ was proposed in the context of urea kinetic modeling (UKM), where the change in concentration of urea ($C$) could be predicted from $K$, generation rate ($G$) and $V$. Similarly, $G$ and $K_t/V$ could be calculated from the change in $C$. $V$ or $K$ can also be calculated by UKM if the other is known. UKM is useful for trouble shooting and quality control of intermittent dialysis as differences between expected and delivered $K_t/V$ expose problems with the dialysis process.

Another type of $K_t/V$, the equilibrated $K_t/V$ ($eK_t/V$) accounts for the transfer of urea within the patient and the post-dialysis rebound. The $eK_t/V$ is always lower than $K_t/V$, and the difference is greater with shorter dialysis sessions, which have a greater post-dialysis rebound.

Later, $K_t/V$ was applied to peritoneal dialysis (PD) [3]. In this case, $t$ is set to an arbitrary interval (usually 1 week). Since $C$ is relatively stable, UKM is not possible and $V$ is estimated using anthropometric methods (e.g. Watson) or measured using bioimpedance. $V$ calculated in dialysis patients using bioimpedance is up to 30% lower than when predicted using Watson. $V$ calculated using bioimpedance agrees with $V$ calculated by UKM [4].

In a typical HD patient, blood urea concentrations during the entire week are more influenced by the urea generation rate ($G$), duration of the periods between dialysis and any renal function than they are by $K_t/V$. Therefore, $K_t/V$ is not useful in comparing different types of dialyses and schedules. Schedules with shorter intervals between dialysis (e.g. long nocturnal, daily) result in a lower weekly peak and time average urea concentrations (TACs) than standard thrice-weekly dialysis despite similar $K_t/V$ multiplied by the number of sessions per week. With thrice-weekly dialysis, in an anuric patient, even an infinite $K_t/V$ would result in lower TAC than 12 mL/min of continuous urea clearance (e.g. by renal function).

For a more realistic comparison of clearance delivered with varying schedules and taking renal function into account, the standard $K_t/V$ (std$K_t/V$) has been proposed [5]. This quantifies dialysis as $G$ divided by the average peak (pre-dialysis) concentration calculated by UKM. In an individual patient, treatments resulting in the same std$K_t/V$ but with different schedules or even continuous treatments would have the same average peak urea concentrations. However, TAC and the highest peak concentration would still be higher in more intermittent treatments [6]. The unphysiological variations in concentration due to intermittent dialysis are also not taken into account in std$K_t/V$, but could be quantified as the time average deviation (TAD) [7].

Alternative continuous dose measures are calculated from $G$ in the same way as std$K_t/V$, but use different, possibly more clinically relevant, measures of concentration than the average peak. The solute removal index (SRI) [8] uses the highest peak urea concentration. The equivalent renal urea clearance (EKR)
### Table 1. Different measures of dialysis dose

<table>
<thead>
<tr>
<th>Dose measure</th>
<th>Measure of;</th>
<th>Method</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>sp(K_t/V) Single-pool (K_t/V) [2]</td>
<td>Session of HD</td>
<td>Calculated using UKM</td>
<td>Dimensionless</td>
</tr>
<tr>
<td>(eK_t/V) Equilibrated (K_t/V)</td>
<td>Session of HD</td>
<td>sp(K_t/V) using the equilibrated (30 min) post-dialysis urea.</td>
<td>Dimensionless</td>
</tr>
<tr>
<td>(K_t/V) (PD) [3]</td>
<td>Week of PD and/or Renal clearance</td>
<td>(K \times 10,080/V)</td>
<td>Weeks(^{-1})</td>
</tr>
<tr>
<td>Creatinine clearance (PD)</td>
<td>Week of PD and/or Renal clearance</td>
<td>(K_c \times 10,080 \times 1.73/SA) ((K_c = ) creatinine clearance, (SA = ) surface area)</td>
<td>L/week/1.73 m(^2)</td>
</tr>
<tr>
<td>Renal creatinine clearance (non-dialysis patients)</td>
<td>Renal clearance</td>
<td>(Kc \times 1.73/SA)</td>
<td>mL/min/1.73 m(^2)</td>
</tr>
<tr>
<td>std(K_t/V) Standard (K_t/V) [5]</td>
<td>Week of HD, PD and/or renal clearance</td>
<td>(G \times 10,080/V/Cap) (Cap = average pre-dialysis urea concentration)</td>
<td>Weeks(^{-1})</td>
</tr>
<tr>
<td>SAN-sp(K_t/V) SAN-(eK_t/V) SAN-std(K_t/V) Surface area normalized (K_t/V) [17]</td>
<td>Session of HD Week of HD, PD and/or renal clearance.</td>
<td>SAN-(K_t/V = K_t/V \times V/SA)</td>
<td>L/m(^2) L/m(^2)/week</td>
</tr>
<tr>
<td>EKR equivalent renal clearance [9]</td>
<td>HD, PD and/or renal clearance</td>
<td>G/TAC (TAC = time average urea concentration)</td>
<td>mL/min</td>
</tr>
<tr>
<td>EKRc volume-corrected EKR</td>
<td>HD, PD and/or renal clearance</td>
<td>EKR \times V/40</td>
<td>mL/min/40l</td>
</tr>
<tr>
<td>SRI solute reduction index [8]</td>
<td>Week of HD, PD and/or renal clearance</td>
<td>(G \times 10,080/V/Cp) ((C_p = ) peak urea concentration)</td>
<td>Weeks(^{-1})</td>
</tr>
<tr>
<td>TAD/TAC [7]</td>
<td>Urea concentration, taking intermittency of dialysis into account</td>
<td>TAC, TAD (TAD = average absolute deviation from TAC)</td>
<td>mmol/L or mg/dL</td>
</tr>
</tbody>
</table>

### Table 2. Different methods for \(K_t/V\) approximation

<table>
<thead>
<tr>
<th>Approximation</th>
<th>Equation</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>sp(K_t/V) [13]</td>
<td>(K_t/V = -\text{Ln}(R - 0.008 \times t) + (4-3.5 \times R) \times 0.55 \times UF/W) ((R = Cpre/Cpost, UF = ultrafiltered volume, W = body weight)</td>
<td>Accurate only in thrice-weekly dialysis and with samples taken at the midweek or the end of week session.</td>
</tr>
<tr>
<td>sp(K_t/V) [1]</td>
<td>(K_t/V = -\text{Ln}(R - \text{GFAC} \times t) + (4-3.5 \times R) \times 0.55 \times UF/W) ((\text{GFAC} = ) adjustment factor for G)</td>
<td>GFAC varies according to the frequency of dialysis and duration of the preceding interdialytic interval.</td>
</tr>
<tr>
<td>Renal component of sp(K_t/V) (3×/week HD) [16]</td>
<td>(KrU \times 4500/V) ((\text{KrU} = ) renal urea clearance)</td>
<td>Approximate adjustment of std(K_t/V) to account for the effect of renal function in the interdialytic interval.</td>
</tr>
<tr>
<td>(eK_t/V) [13]</td>
<td>(eK_t/V = spK_t/V\times 0.6 \times K_t/V + 0.03)</td>
<td>Prediction can be used for any solute by using a solute-specific value for td ((\text{e.g. td} = 30 \text{ for urea, } 70 \text{ for creatinine, } 110 \text{ for b2microglobulin})).</td>
</tr>
<tr>
<td>(eK_t/V) [14]</td>
<td>(eK_t/V = spK_t/V \times (t/td))</td>
<td>Prediction can be used for any solute by using a solute-specific value for td ((\text{e.g. td} = 30 \text{ for urea, } 70 \text{ for creatinine, } 110 \text{ for b2microglobulin})).</td>
</tr>
<tr>
<td>std(K_t/V) [15]</td>
<td>(\frac{\text{std}K_t}{V} = \frac{10080 \times (1 - e^{-ek_t/V}/t)}{1 - e^{-ek_t/V} / (eK_t/V) + (10080/N_v) - 1})</td>
<td>Does not account fully for ultrafiltration or renal function.</td>
</tr>
</tbody>
</table>
Therefore, renal urea clearance is \( \sim50\% \) of GFR and considerably underestimates the clearance of most other solutes [24].

The terminology for quantifying dialysis dose is confusing, with different types of \( K_t/V \), some with different units (Table 1). Despite using mathematics, with the potential for calculating reproducible and consistent results from the same inputs, we are using approximate methods which produce different results from the same inputs, depending on the method used.

We need a standard method for calculating dialysis dose, taking all the required factors into account. This would be a dialysis-equivalent GFR. It should, ideally, preserve the advantages of UKM but extended or extrapolated to more representative solutes. It should be consistent with the terminology used for quantifying renal function, normalized using the surface area rather than \( V \) and account for average toxin concentrations as well as the unphysiological deviations due to intermittent dialysis.

(See related article by Daugirdas et al. Improved equation for estimating single-pool \( K_t/V \) at higher dialysis frequencies. *Nephrol Dial Transplant* 2013; 28: 2156–2160.)

---

**REFERENCES**

5. Gotch FA. The current place of urea kinetic modeling with respect to different dialysis modalities. *Nephrol Dial Transplant* 1998; 13: 10–14
6. Daugirdas JT, Tattersall J. Effect of treatment spacing and frequency on three measures of equivalent clearance, including standard \( K_t/V \). *Nephrol Dial Transplant* 2010; 25: 558–61
7. Lopot F, Nejedly B, Sulkova S. Physiology in daily hemodialysis in terms of the time average concentration/time average deviation concept. *Hemodial Int* 2004; 8: 39–44
12. Termorshuizen F, Dekker FW, van Manen JG *et al.* NECOSAD Study Group. Relative contribution of residual renal function and

Received for publication: 3.10.2012; Accepted in revised form: 11.4.2013

doi: 10.1093/ndt/gfs446
Advance Access publication 18 December 2012

**Peritoneal fibrosis is mouse strain dependent**

Tanya Bodenham,
Nicholas Topley
and Donald Fraser

**Correspondence and offprint requests to:** Donald Fraser; E-mail: fraserj@cf.ac.uk

Peritoneal dialysis is a widely used mode of renal replacement therapy in which preservation of the structural and functional integrity of the peritoneal membrane is critical for continued success. Progressive scarring, or fibrosis, in the peritoneal membrane is now well described in peritoneal dialysis patients, but its extent is variable. While some patients survive for long periods on peritoneal dialysis, others suffer from ‘fibrosis-related’ membrane failure, or rarely, more severe complications such as encapsulating peritoneal sclerosis (EPS). The reasons for these variations in responses are unlikely to be explained by variations in the therapy, which has remained largely unchanged over the past 20 years, and are suggestive of a genetic component to the susceptibility of individuals to different outcomes. In this issue of NDT, Margetts et al. [1] describe how they used genetically different mouse strains to examine the variability in responses to a defined, constant pro-fibrotic stimulus in a model of peritoneal fibrosis. The data highlight a possible genetic linkage to susceptibility to fibrosis that adds significant insights into our understanding of the mechanisms driving peritoneal damage.

The key to continued success of peritoneal dialysis as a therapy remains in preservation of the performance of the peritoneal membrane as a dialysing organ. In health, the visceral and parietal peritoneum and its phospholipid-rich secretions and anti-friction surfaces facilitate bowel motility within the abdominal cavity. The outer surface of the whole comprises a single layer of mesothelial cells, specialized to provide a low friction and non-adhesive surface. The mesothelium that lines