



# Principles of Renal Function Measurement (Limitations of Gotch's Kt/V)

Canadian Journal of Kidney Health  
and Disease  
Volume 5: 1–4  
© The Author(s) 2018  
Reprints and permissions:  
sagepub.co.uk/journalsPermissions.nav  
DOI: 10.1177/2054358118776020  
journals.sagepub.com/home/cjk



Michael Bonert<sup>1</sup> and Bradley A. Saville<sup>2</sup>

## Abstract

Kt/V is a nondimensional number and a scaling parameter that has, with arbitrary definitions, been recast as a measure of dialysis by Gotch and Lysaght. This editorial discusses the concept of nondimensional numbers within the context of dialysis measurement, modeling, and medical evidence. It concludes that Gotch's Kt/V, Lysaght's Kt/V, and standardized Kt/V are not well suited to measure dialysis. An ideal dialysis measure would be proportional to toxins cleared by the kidney, portable with regard to dialysis modality, practical (largely devoid of calculations) and reflective of the pathology/physiology.

## Abrégé

Le Kt/V est un nombre non dimensionnel et un paramètre de dispersion qui, selon des définitions arbitraires, est devenu une mesure de l'efficacité de la dialyse avec Gotch et Lysaght. Le présent éditorial discute du concept de nombre non dimensionnel dans le contexte de la mesure de l'efficacité de la dialyse, de la modélisation et de la médecine factuelle. L'article conclut que le Kt/V de Gotch, le Kt/V de Lysaght et le Kt/V standardisé sont inadéquats pour la mesure de l'efficacité de la dialyse. En effet, une mesure idéale de l'efficacité de la dialyse serait proportionnelle aux toxines éliminées par les reins, adaptable à la modalité de dialyse, facile à utiliser (largement dénuée de calculs) et représentative de la pathologie/physiologie du patient.

## Keywords

Kt/V, kinetic modeling, Buckingham Pi Theorem, nondimensional numbers, dialysis adequacy, renal function measurement

Received October 29, 2017. Accepted for publication February 24, 2018.

## What was known before

A nondimensional analysis can provide additional insight into the behavior of a complex system.

## What this adds

The Buckingham Pi Theorem connects kinetic modeling in nephrology with an older and larger well-developed body of literature on modeling in engineering and physics and provides additional insights into dialysis and renal function measurement.

This work proposes 4 principles for evaluating measures of renal function and renal replacement therapies (proportional, practical, portable, and physiological/pathological).

## Introduction

Having closely examined dialysis measurement, it is our perspective that the great deal of mathematics in dialysis measurement is challenging to comprehend and master for

many nephrologists. Aware of the audience and our goal of reaching the largest possible audience, we will heed advice given to Stephen Hawking (when he was writing his now famous books about space & time) and strive to avoid formulas—aware that for every formula, we probably lose readership. We will stick to the concepts in words and endeavor to explain dialysis modeling in simple terms. We will discuss measurement, where Kt/V comes from, why it will not go away completely, and modeling. Then, we will outline what we believe should be basic principles in dialysis measurement.

<sup>1</sup>St. Joseph's Healthcare Hamilton, McMaster University, Hamilton, Ontario, Canada

<sup>2</sup>University of Toronto, Chemical Engineering and Applied Chemistry, Toronto, Ontario, Canada

## Corresponding Author:

Michael Bonert, Department of Department of Pathology, St. Joseph's Healthcare Hamilton, Room L206, 50 Charlton Avenue East, Hamilton, Ontario, Canada L8N 4A6.

Email: bonertm@mcmaster.ca



## Measurement

Objectively measuring something that is useful is accomplished by (1) knowing that what you are measuring is meaningful and (2) being able to measure it with some accuracy. Nephrology has struggled a good deal with the former question (“what to measure?”) and it is our opinion that Kt/V made the trip from the biomedical engineering literature to the nephrology literature—because of it. The national cooperative dialysis study (NCDS) study in the 1970s was essentially a failure, as it was based on urea. Gotch and Sargent managed to salvage some useful information out of it because of their analysis.<sup>1</sup> At the time, it was a valuable contribution. The problem is that it was thereafter contorted to become a dialysis measure. Urea itself is not a toxin. Its measurement is a product of history; it does not provide any deeper insights into the pathology of renal failure. The urea level itself is not particularly useful—it is the change that is informative, and that change in understanding improved lives; nephrologists in the past suggested to their patients they should not eat meat/protein (as it will raise their urea level) and a number of those patients were likely more miserable and more malnourished as a consequence. The second part (“measuring something accurately”) is complicated if you are measuring a change in urea, as the postdialysis concentration rebound has to be accounted for. Given the above complexity, we find it understandable that some nephrologists want to forego measurement altogether and use clinical judgment. However, we believe measurement makes sense and is an objective way to compare outcomes. The question is, “What to measure?” A predialysis concentration of a toxin or set of toxins? We do not have the answer, but it seems prudent to move beyond urea if we want to effectively manage dialysis patients.

## Kt/V

Kt/V is a term that shows up in equations that model both hemodialysis and peritoneal dialysis. It applies to any substance (toxin, drug) cleared by these modalities; however, it should be noted that the clearance (K) and volume of distribution (V) values are different for different toxins, and dependent on the modality. The small “t” (in hemodialysis) represents the dialysis time. The volume of distribution divided by the clearance (V/K) has units of time and represents the time elapsed for the predialysis concentration to go 63% of the way to a (hypothetical) steady state concentration. In renal patients, the steady state concentration (the toxin generation rate divided by the clearance) is never reached (in hemodialysis) due to practical considerations. However, it is useful to understand that this represents the concentration that would be reached if one hooked up a patient to the dialysis machine for a “long time.” Practically speaking, a “long time” is if one were to dialyze a patient for a duration greater than 5 times the V/K value (Kt/V greater than 5), because, at this point, the difference between the

theoretical steady state value and concentration would be less than 1%. Kt/V by itself (without information about dialysis frequency, toxin generation rate, and residual renal function) is insufficient to say anything about toxin concentration, and this is why Gotch came up with “standardized Kt/V,” which is really a measure of concentration.

## Gotch’s Kt/V

Gotch’s Kt/V contorts the well-established engineering principles that underpin the use of scale models, a subject we previously discussed in a biomedical engineering journal.<sup>2</sup> At a practical level, scaling was understood over a 100 years ago. In 1914, the underlying theory was rigorously proven by Buckingham<sup>3</sup> and is now known as the Buckingham Pi Theorem. Buckingham’s theorem has its basis in one simple fact: the algebra for the physical (base) units (eg, meter, second, mole) has to work if the equation is valid. This may not seem obvious, but is actually one of the most important underpinnings of all modeling/analysis work in engineering, physics, and medicine. One consequence of this is that all nonempirical equations can be mathematically rearranged to result in ratios where the units cancel, resulting in nondimensional numbers. Kt/V is one such nondimensional number. There are many others, although to a layperson, many are obscure. The best-known ratio outside of engineering is probably the Mach number (the speed in relation to the speed of sound), or perhaps the G-force. To define a patient’s physiology, in hemodialysis, one needs (in addition to Kt/V) at least 2 other nondimensional numbers (if the residual function is zero). One is concentration times clearance divided by toxin generation rate (CK/G), which not coincidentally looks a bit like the Cockcroft-Gault equation ( $K = G/C$ ). The second is the ratio between the dialysis time (t) and the interval between the start of dialysis sessions (T). An important alternate nondimensional group to CK/G is CV/GT. Physically, CV/GT is the concentration divided by the anephric concentration rise during the time interval between the start of dialysis sessions, “T.” The Gotch’s standardized Kt/V is similar to this group; in a simple form, standardized Kt/V is directly proportional to G/CV. If residual renal function (Kr) is considered, a fourth nondimensional group is required, such as KrT/V.

## Utility of Nondimensional Groups

Seen practically, the importance of nondimensional groups is (1) they allow one to mathematically simplify a problem considerably, and (2) if the nondimensional groups match, it is possible to properly scale experimental results. One can also plot nondimensional groups against one another and use that to understand the relationship between parameters (eg, residual renal function versus toxin concentration) without doing significant calculations; however, reading these types of plots does take some practice.<sup>2</sup>

In the context of dialysis, Gotch's NCDS post hoc analysis (using  $Kt/V$ ) can be understood as an exercise in scaling, like those done to get results from measurements done on a scale model in a wind tunnel. The reason that patients with similar  $Kt/V$  values have similar outcomes is that this is a scaling parameter, and for the same reason, scaling parameters allow the aerodynamics of supersonic aircraft to be predicted from scale models. However, we point out that the nondimensional scale parameter has to be appropriate for the system. Gotch's matching of the  $Kt/V$  was an adjustment that (for conventional hemodialysis) removed variability due to clearance ( $K$ ), volume of distribution ( $V$ ), and dialysis time ( $t$ ); it is on a firm theoretical basis. It is unfortunate that  $Kt/V$  was misused thereafter—touted as a way to measure dialysis, and subsequently re-defined by Gotch and Lysaght in a way that creates a number of problems which we will now go on to elucidate.

Gotch defined  $Kt/V$  as a function of the predialysis and postdialysis urea concentration; this differs from how " $Kt/V$ " (the product of " $K$ " and " $t$ " divided by " $V$ ") is defined within the context of nondimensional scaling, following the principles of the Buckingham Pi Theorem. The results of Gotch's definition are (1) Gotch's  $Kt/V$  is lower with more frequent dialysis, (2) Gotch's  $Kt/V$  equals zero for continuous dialysis, (3) the standardized  $Kt/V$ - $Kt/V$  plots (known as the " $Kt/V$  nomogram") give nonsensical results for long dialysis times (demonstrated in detail in our prior paper), and (4) (Gotch's)  $Kt/V$  is essentially a misnomer. Based on Buckingham's approach, one should see  $Kt/V$  as the product of clearance and time divided by the volume of distribution; Gotch defines  $Kt/V$  as a complicated (transcendental) function of a concentration ratio. The Buckingham  $Kt/V$  is representative of the dialysis process/system and is, thus, useful for scaling; in contrast, Gotch's complicated concentration function approximates the correct result for conventional hemodialysis, but fails for other modalities and other conditions.

The  $Kt/V$  for peritoneal dialysis (as defined by Lysaght<sup>4</sup>) is not a nondimensional number at all. It is (the inverse of) the urea concentration cleansed of the protein intake/generation effects ( $G/CV$ ). It is more closely related to standardized  $Kt/V$  than the  $Kt/V$  for hemodialysis. Lysaght's sleight of hand with the units is something that is much frowned upon in engineering because the algebra of the units is a way to check a calculation. If the algebra for the units in a calculation is wrong, the answer is usually wrong!

## Modeling and Dialysis Measurement

Unfortunate in all of this is that the results of the modeling appear to have had a limited impact on how nephrologists think about theoretical approaches to better understand pathophysiology with some validation vis-à-vis large trials. Modeling allows one to predict toxin concentrations reasonably well, given the parameters of the dialysis prescription

and the patient's physiologic parameters. The effect of residual renal function was thus long under-appreciated. Short, frequent dialysis is more effective and longer dialysis is more effective. These findings could have been predicted using the properly constructed model equations, along with the toxin concentrations from which morbidity and mortality could have been estimated.

The larger issue, and this applies to all of medicine, is physicians' unease with modeling. The reasons for this include a lack of teaching about modeling in the medical school curriculum and an antireductionist philosophy (the idea that models cannot represent the complexity of a system—particularly a system as complex as the human body). The philosophical debate (reductionism vs antireductionism) is quite old and we will not delve into it much further than stating our belief: progress is largely built on reductionism; although complex, the function of various organs in the human body is governed by physical, chemical, and biological principles that, when reasonably understood, form the foundation for a sound model of the system. Furthermore, we believe that the principles of modeling can be understood without learning a lot of mathematics and are confident that modeling will become more accepted over time. Using models requires (1) understanding the modeling assumptions, (2) understanding the parameter range for which a model is applicable, and (3) having quality (experimental) data that allows one to validate the model and understand conditions that may lead to deviations from the model. In engineering, aerodynamics (and fluid dynamics more generally) was largely an experimental field several decades ago. Today, much of the "experimentation" is done via modeling with a small amount of experimental validation. The modeling work in fluid dynamics (along with modeling of heat transfer and solid mechanics) has allowed engineers to, for example, make durable jet engine combustors that contain gases that are hotter than the melting temperature of the combustor housing. Concepts such as flux balance analysis in combination with genetics and other biomarkers are leading the path toward personalized medicine and nutrigenomics. Modeling complex microbial communities in the gastrointestinal tract is seen as key to developing new therapeutics and better understanding the impact of diet on various diseases. Finally, recent Nobel prizes in chemistry have gone to researchers focused on modeling work.

## Modeling Is a Tool to Achieve a Goal

Modeling is the means to an end not an end in itself. Model structures and assumptions should lead to accurate predictions of toxin concentrations and the fluid balance. However, the details of the calculation should be secondary to the measured target values (which should predict outcome). Measurement-based target values should be at the center of discussions on dialysis adequacy. Blood sugar in a diabetic

can be optimized or controlled with various interventions (eg, lifestyle modification, obesity surgery, oral drugs, insulin injections, insulin pump). The measurement is essentially the same regardless of the intervention. We think the same should broadly apply in the measurement of renal function and renal replacement therapies. A good model must be consistent with outcomes or trends that a seasoned nephrologist understands intuitively, through experience and clinical practice. In addition, a well-structured model can help inform the practitioner about additional, perhaps nonintuitive “levers” that can be manipulated to manage uremic toxins, and the likely magnitude of the response. Furthermore, a well-structured model will predict consistent trends and outcomes for different treatment modalities, eg, whether hemodialysis or peritoneal dialysis.

### Evidence-Based Medicine and Modeling

In the context of evidence-based medicine, we suspect “modeling” with selected validation, in most cases, would fit under “expert opinion,” and “expert opinion” is seen as the least reliable form of (medical) evidence.<sup>5</sup> However, modeling is the basis for how many things are done in engineering; the buildings generally do not collapse, and airplanes with millions of parts fly reliably, because the models have captured the essential elements of the system. In the context of nephrology, a good deal of the literature on dialysis adequacy could have been done better with modeling and validation. Both the NCDS and HEMO study suggested that longer dialysis is not useful—yet, that is the opposite of what the kinetics modeling suggests! Data from long nocturnal hemodialysis certainly are in line with the kinetics modeling and physical basis of the system, yet it appears to be viewed with skepticism by some physicians because there are not thousands of patients involved in those studies.

### Conclusion

With an appreciation of where Kt/V comes from and what it represents, it is clear that it does not represent a good way to measure dialysis. It is impractical as it is nontrivial to calculate. Comparison with normal renal function and various dialysis modalities is essentially precluded, as the definitions for peritoneal dialysis and hemodialysis are different. Confounding comparisons is the fact that Kt/V has an inverse relationship to toxin concentrations—which are more difficult to readily compare and understand. The measures (Kt/V, standardized Kt/V) do not reflect the pathology of end-stage renal disease.

Considering the statements above, we propose that principles of dialysis measurement should be based on the 4 Ps:

1. Proportional: the measures should be proportional to the toxins, not an inverse
2. Practical: the measures should be easy to interpret and should not require extensive calculations
3. Portable: the measure should be portable with regard to dialysis modality, ie, not dependent on the renal replacement modality
4. Physiological/pathological: the measures should reflect the pathologic process

Kt/V fails on all 4 principles!

Kt/V provides insight into what is happening physiologically; however, it is insufficient to describe the system completely. Kt/V should be understood properly as a number that is analogous to the half-life in radioactive decay. It is a scaling parameter that allowed useful information to be extracted from the NCDS. Progress in nephrology will be accelerated when the basis for and limitations of Kt/V are better understood, and we move beyond Kt/V as a measure of dialysis efficacy.

### Ethics Approval and Consent to Participate

Not required.

### Consent for Publication

Not required.

### Availability of Data and Materials

Not required.

### Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

### Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

### References

1. Gotch FA, Sargent JA. A mechanistic analysis of the National Cooperative Dialysis Study (NCDS). *Kidney Int.* 1985;28:526-534.
2. Bonert M, Saville BA. A non-dimensional analysis of hemodialysis. *Open Biomed Eng J.* 2010;4:138-155.
3. Buckingham E. The principle of similitude. *Nature.* 1915;96:396-397.
4. Lysaght MJ, Pollock CA, Hallet MD, Ibels LS, Farrell PC. The relevance of urea kinetic modeling to CAPD. *ASAIO Trans.* 35;1989:784-790.
5. Guyatt GH, Sackett DL, Sinclair JC, Hayward R, Cook DJ, Cook RJ. Users' guides to the medical literature. IX. A method for grading health care recommendations. Evidence-Based Medicine Working Group. *JAMA.* 1995;274:1800-1804.