Hospital General Universitario
Santa Lucía

16.50 -18.50 h.

MESA REDONDA HEMODÍALISIS CONTROVERSIAS

Moderadores:

Dra. María Jesús Camba Caride. C.H. U. de Ourense

Dr. Secundino Cigarrán Guldris. H. da Costa de Burela

MÁS ALLA DE KT/V O KT. ÚLTIMOS DÍAS DEL KT/V?

Pro: Dr. Manuel Molina Núñez. H.G. U. Sta. Lucía de Cartagena

Contra: Dr. José Luis Teruel Briones. H. U. Ramón y Cajal de Madrid

M. Molina Núñez

Jefe de Servicio de Nefrología

Complejo Hospitalario Universitario Cartagena

Ourense, 28 de octubre de 2016

mini review

http://www.kidney-international.org

Once upon a time in dialysis: the last days of Kt/*V*?

Raymond Vanholder[1], Griet Glorieux[1] and Sunny Eloot[1]

[1]*Nephrology Section, Department of Internal Medicine, Ghent University Hospital, Ghent, Belgium*

After its proposal as a marker of dialysis adequacy in the eighties of last century, Kt/V_{urea} helped to improve dialysis efficiency and to standardize the procedure. However, the concept was developed when dialysis was almost uniformly short and was applied thrice weekly with small pore cellulosic dialyzers. Since then dialysis evolved in the direction of many strategic alternatives, such as extended or daily dialysis, large pore high-flux dialysis, and convective strategies. Although still a useful baseline marker, Kt/V_{urea} no longer properly covers up for most of these modifications so that urea kinetics are hardly if at all representative for those of other solutes with a deleterious effect on morbidity and mortality of uremic patients. This is corroborated in several clinical studies showing a dissociation between removal of urea and that of other uremic toxins. In addition, randomized controlled trials showed no benefit of increasing Kt/V_{urea}. Finally, this parameter also hardly is evocative for metabolic or intestinal generation of toxins, for their removal by residual renal function and for the complex interaction of dialysis length with removal pattern and patient outcomes. We conclude that apart from being a baseline parameter of dialysis adequacy, Kt/V_{urea} insufficiently represents all novel strategic changes of modern dialysis. Kt/V_{urea} is too simple a concept for the complexities of uremia and of today's dialysis.

Kidney International (2015) **88**, 460–468; doi:10.1038/ki.2015.155;
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KEYWORDS: hemodialysis; urea; uremia; uremic toxins

Kt/V_{urea} (clearance of urea multiplied by dialysis duration and normalized for urea distribution volume) was first proposed as a parameter of dialysis adequacy in a period of worrisome mortality on dialysis in the USA. After the randomized National Cooperative Dialysis Study had demonstrated that a higher time averaged urea concentration was related to higher hospitalization,[1] Kt/V_{urea} emanated from a post hoc mechanistic study on the same data.[2] The threshold of this absolute value was originally set at 0.8 but soon was increased to 1.2 or higher. With the introduction of Kt/V_{urea}, adequacy of dialysis was no longer assessed by a single static pre-dialysis value, of which the low concentration could be due to negative confounders such as low protein intake for urea or low muscle mass for creatinine. Kt/V_{urea} instead is a dynamic parameter that assesses removal by dialysis as a whole (Kt), including not only clearance but also dialysis length and above all a correction for body mass (*V*). For the first time not only the therapy but also the patient was taken into account by acknowledging that a voluminous person needs more dialysis compared with a tiny one. This led to a more standardized dialysis approach and was translated into a better survival with higher Kt/V_{urea} in essentially observational studies.[3,4]

However, Kt/V_{urea} quite soon appeared to be far from the only determinant of outcomes of dialysis. A study by Owen *et al.*[5] demonstrated a relation between urea reduction ratio (as surrogate for Kt/V_{urea}) and outcomes, but a much stronger consistent relationship was found for hypoalbuminemia, as an index of malnutrition and fluid overload. In an analysis of the Dialysis Outcomes Practice Pattern Study, dialysis length appeared an important determinant of survival, even in patients stratified for Kt /V_{urea}.[4]

When different thresholds of Kt/V_{urea} were compared in controlled trials, increasing its value above standard did not impact survival,[6,7] suggesting that the upper limit of improving outcomes based on this parameter had been reached. This raised the question whether Kt/V_{urea} can grasp all effects of modern dialysis in all its variants and also which potential pitfalls skew its interpretation.

Kidney International, Vol. 63 (2003), pp. 1934–1943

Review on uremic toxins: Classification, concentration, and interindividual variability

Table 3. Middle molecules ($N = 22$)

Solute	Group
Adrenomedullin *ng/L*	Peptides
Atrial natriuretic peptide *ng/L*	Peptides
β_2-microglobulin *mg/L*	Peptides
β-endorphin *ng/L*	Peptides
Cholecystokinin *ng/L*	Peptides
Clara cell protein (CC16) *mg/L*	
Complement factor D *mg/L*	Peptides
Cystatin C *mg/L*	Peptides
Degranulation inhibiting protein I[c]	Peptides
Delta-sleep inducing peptide *μg/L*	Peptides
Endothelin *ng/L*	Peptides
Hyaluronic acid *μg/L*	Peptides
Interleukin-1β *ng/L*	Cytokines
Interleukin-6 *ng/L*	Cytokines
κ-Ig light chain *mg/L*	Peptides
λ-Ig light chain *mg/L*	Peptides
Leptin *μg/L*	Peptides
Methionine-enkephalin *ng/L*	Peptides
Neuropeptide Y *ng/L*	Peptides
Parathyroid hormone *μg/L*	Peptides
Retinol-binding protein *mg/L*	Peptides
Tumor necrosis factor-α *ng/L*	Cytokines

Abbreviations are: C_N, normal concen
The underlined numbers behind the sla
no data about the number of samples w
a single value as a maximum (accompar
[a] C_{MAX} values are original data (all oth
[b] S Schmaldienst, Vienna: personal co
[c] Degranulation inhibiting protein 1 c

Spermine *μg/L*

Abbreviations are: C_N, normal concentration, [illegible] ref, reference; CMPF, 3-carboxy-4-methyl-5-propyl-2-furanpropionic acid; AGE, advanced glycation end products. The underlined numbers behind the slash point to the number of data on which the means or medians have been obtained. No underlined number indicates that no data about the number of samples were available. Normal values are reported as means ± SD, or in the case of a single value as a maximum (accompanied by <); uremic values are reported as means ± SD.

[a] C_{MAX} values are original data (all other values were calculated as mean + 2 SD based on C_U).

Table 7. Solutes to be considered for the future

1-alkyl-2-formyl-3,4-glycosyl-pyrrole
2-(2-fuoryl)-4(5)-(2-furanyl)-1H-imidazole
3-deoxyfructosone
3-hydroxykinurenine
4-hydroxynonenal
Advanced oxidation protein products (AOPP)
Advanced glycation end products-β_2-microglobulin
Anthranilic acid
β_2-microglobulin fragments
Cadaverine
Crossline
Dimethylamine
Guanosine
Imidazolone
Malonaldehyde
Malondialdehyde
Methylamine
N^{ε}-carboxyethyllysine
Organic chloramines
Oxidized low-density-lipoprotein (oxLDL)
Parathyroid hormone fragments
Pyrraline
Pyrrole aldehyde
Trimethylamine

ref, reference.
indicates that
in the case of

Polyamines

Solute

1-methylad
1-methylgu
1-methylinc
ADMA *mg*
α-keto-δ-gu
α-*N*-acetyla
Arab(in)ito
Argininic a
Benzylalcol
β-guanidino
β-lipotropir
Creatine *m*
Creatinine
Cytidine *μg*
Dimethylgl
Erythritol
γ-guanidino
Guanidine
Guanidinoa
Guanidono
Hypoxanthi
Malondiald
Mannitol *m*
Methylguar
Myoinositol
N^2,N^2-dimet
N^4-acetylcyt
N^6-methyla
N^6-threonyl
Orotic acid
Orotidine
Oxalate *mg*
Phenylacety
Pseudourid
SDMA *μg/*
Sorbitol *mg*
Taurocyam
Threitol *μg*
Thymine *m*
Uracil *μg/L*
Urea *g/L*
Uric acid *m*
Uridine *mg/*
Xanthine *m*
Xanthosine

Abbreviatic
ADMA, asym
means or medians have been obtained. No underlined number indicates that no data about the number of samples were available. Normal values are reported as means ± SD, or in the case of a single value as a maximum (accompanied by <); uremic values are reported as means ± SD or, in the case of a single value, as a median.

[a] C_{MAX} values are original data (all other values were calculated as mean + 2 SD based on C_U)

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mini review

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Once upon a time in dialysis: the last days of Kt/*V*?

Raymond Vanholder[1], Griet Glorieux[1] and Sunny Eloot[1]

[1]Nephrology Section, Department of Internal Medicine, Ghent University Hospital, Ghent, Belgium

Kt/V_{urea} (clearance of urea multiplied by dialysis duration and normalized for urea distribution volume) was first proposed as a parameter of dialysis adequacy in a period of worrisome mortality on dialysis in the USA. After the randomized National Cooperative Dialysis Study had demonstrated that a higher time averaged urea concentration was related to higher hospitalization,[1] Kt/V_{urea} emanated from a post hoc mechanistic study on the same data.[2] The threshold of this absolute value was originally set at 0.8 but soon was increased to 1.2 or higher. With the introduction of $Kt/V_{urea,}$ adequacy of dialysis

outcomes based on this parameter had been reached. This raised the question whether Kt/V_{urea} can grasp all effects of modern dialysis in all its variants and also which potential pitfalls skew its interpretation.

THE CONCEPT OF KT/V_{UREA} IS BASED ON A TYPE OF DIALYSIS THAT IS OFTEN NO LONGER APPLIED

Urea kinetic modeling was developed when hemodialysis was applied almost systematically three times weekly with small pore cellulosic dialyzers causing substantial inflammatory reaction. Moreover, the session length of this dialysis was usually short, and as Kt/V_{urea} was conceived in the US

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even shorter (mostly 2.5–3 h) than what was standard elsewhere (4 h).

Since then the dialysis concept has changed markedly, with many alternatives to standard, by the introduction of large pore high-flux dialyzers, convective strategies such as hemodiafiltration, extended dialysis, and frequent dialysis,[8] which all have been shown to better remove molecules with proven biological impact and/or result in better outcomes.[9] The question arises whether Kt/V_{urea} is still representative for the kinetics of solutes preferentially removed by these alternative strategies, which usually have no added value for the removal of urea in contrast to their impact on the elimination of many other solutes.

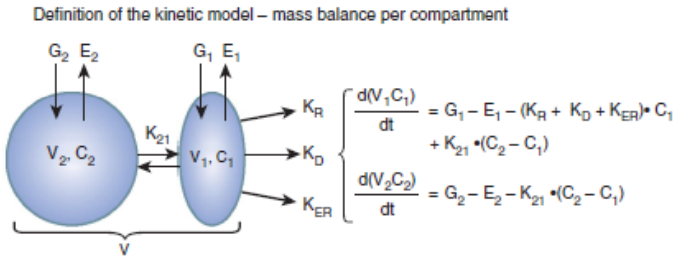

Figure 1 | Basic principles of kinetic modeling. Uremic solute is primarily removed from the plasmatic compartment by dialysis causing a fast decrease in its concentration. Only once this plasmatic concentration starts to decrease sufficiently, concentration in the extra-plasmatic compartment can also decrease, based on a diffusive concentration gradient. C_1 and C_2, solute concentration in V_1 and V_2;

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NEFROLOGÍA. Vol. 25. Suplemento 2. 2005

From adequate to optimal dialysis Long 3 x 8 hr dialysis: a reasonable compromise

B. Charra
Centre de Rein Artificiel de Tassin. France.

Table IV. Standardized Mortality (SMR) vs USRD

Calendar year	O/E* death	SMR	p value
1989	23/43,7	0,53	< 0,005
1990	14/42,4	0,33	< 0,001
1991	18/44,7	0,40	< 0,001
1992	15/46,1	0,33	< 0,001
1993	23/47,7	0,48	< 0,001
1994	20/50,3	0,40	< 0,001
1995	23/57	0,40	< 0,001
1996	27/56,4	0,51	< 0,001
1997	25/48,5	0,52	< 0,001
1998	26/47,6	0,55	< 0,005
1999	27/67,5	0,41	< 0,001
2000	38/71,1	0,53	< 0,001
2001	27/74,1	0,36	< 0,001
2002	32/75,33	0,42	< 0,001
2003	35/70,6	0,50	< 0,001

* O/E = observed/expected deaths.

A comparison of Tassin mortality to the only available long-term French series of 4-5 hr HD reported several years ago[4] shows that long HD mortality was lower (52.4 *vs.* 99 deaths per 1,000 pt-yrs, $p < 0.001$). There was no difference in specific (infection, cancer, or others) causes of death between the 2 series out of CV mortality which was much lower on long HD (29.8 *vs.* 44.6 CV deaths per 1,000 pt-yrs, $p < 0.001$).

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The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 9, 2010 VOL. 363 NO. 24

In-Center Hemodialysis Six Times per Week versus Three Times per Week

The FHN Trial Group*

RESULTS

Patients in the frequent-hemodialysis group averaged 5.2 sessions per week; the weekly standard Kt/V_{urea} (the product of the urea clearance and the duration of the dialysis session normalized to the volume of distribution of urea) was significantly higher in the frequent-hemodialysis group than in the conventional-hemodialysis group (3.54±0.56 vs. 2.49±0.27). Frequent hemodialysis was associated with significant benefits with respect to both coprimary composite outcomes (hazard ratio for death or increase in left ventricular mass, 0.61; 95% confidence interval [CI], 0.46 to 0.82; hazard ratio for death or a decrease in the physical-health composite score, 0.70; 95% CI, 0.53 to 0.92). Patients randomly assigned to frequent hemodialysis were more likely to undergo interventions related to vascular access than were patients assigned to conventional hemodialysis (hazard ratio, 1.71; 95% CI, 1.08 to 2.73). Frequent hemodialysis was associated with improved control of hypertension and hyperphosphatemia. There were no significant effects of frequent hemodialysis on cognitive performance, self-reported depression, serum albumin concentration, or use of erythropoiesis-stimulating agents.

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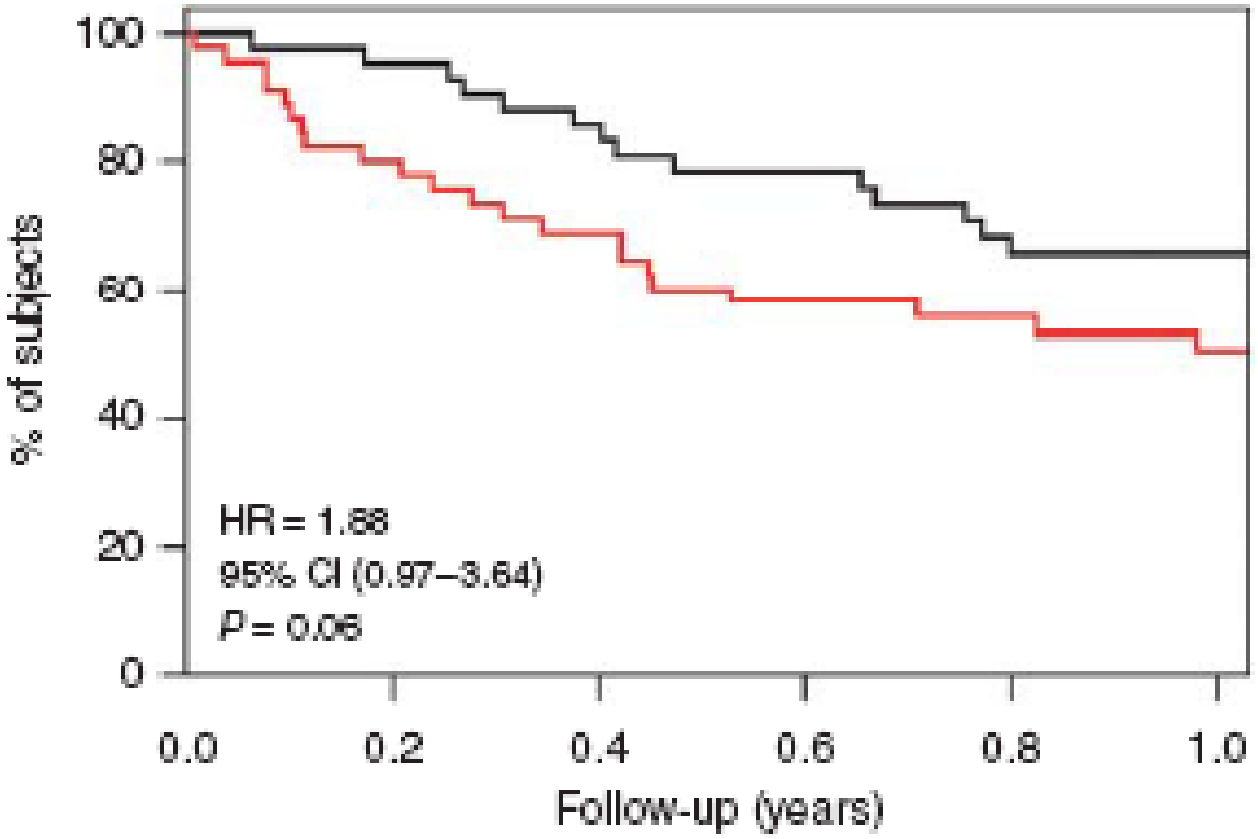
original article http://www.kidney-international.org

see commentary on page 1018

The effects of frequent nocturnal home hemodialysis: the Frequent Hemodialysis Network Nocturnal Trial

Michael V. Rocco[1], Robert S. Lockridge Jr[2], Gerald J. Beck[3], Paul W. Eggers[4], Jennifer J. Gassman[3], Tom Greene[5], Brett Larive[3], Christopher T. Chan[6], Glenn M. Chertow[7,8], Michael Copland[9], Christopher D. Hoy[10], Robert M. Lindsay[11], Nathan W. Levin[12], Daniel B. Ornt[13], Andreas Pierratos[14], Mary F. Pipkin[2], Sanjay Rajagopalan[15], John B. Stokes[16], Mark L. Unruh[17], Robert A. Star[4] and Alan S. Kliger[18], and the Frequent Hemodialysis Network (FHN) Trial Group[19]



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Long Interdialytic Interval and Mortality among Patients Receiving Hemodialysis

Robert N. Foley, M.B., David T. Gilbertson, Ph.D., Thomas Murray, M.S., and Allan J. Collins, M.D.

Table 2. Annualized Mortality and Cardiovascular-Hospitalization Rates.

Event	% of Patients with Event	Rate per 100 Person-Yr (95% CI)			
		Overall	Event Occurred on Day after 2-Day Interdialytic Interval		
			Yes	*No*	*P Value*
Death					
All causes*	41.1	18.6 (18.3–18.9)	22.1 (21.2–23.0)	18.0 (17.7–18.4)	<0.001
Cardiac cause	17.4	7.9 (7.7–8.1)	10.2 (9.6–10.8)	7.5 (7.3–7.7)	<0.001
Vascular cause	2.7	1.2 (1.1–1.3)	1.2 (1.0–1.4)	1.2 (1.1–1.3)	0.9
Infection	4.8	2.2 (2.1–2.3)	2.5 (2.2–2.9)	2.1 (2.0–2.2)	0.007
Other cause	16.3	7.4 (7.2–7.6)	8.2 (7.6–8.7)	7.2 (7.0–7.5)	0.001
Specific causes†					
Cardiac arrest	2.4	1.1 (1.0–1.1)	1.3 (1.1–1.6)	1.0 (0.9–1.1)	0.004
Dialysis withdrawal	4.3	1.9 (1.8–2.1)	2.0 (1.7–2.3)	1.9 (1.8–2.1)	0.8
Myocardial infarction	10.3	4.6 (4.5–4.8)	6.3 (5.8–6.8)	4.4 (4.2–4.5)	<0.001
Septicemia	2.3	1.0 (0.9–1.1)	1.2 (1.0–1.4)	1.0 (0.9–1.1)	0.06
Stroke	1.5	0.7 (0.6–0.8)	0.7 (0.6–0.9)	0.7 (0.6–0.8)	0.8
Cardiovascular hospitalization					
Myocardial infarction	9.0	4.2 (4.1–4.4)	6.3 (5.9–6.9)	3.9 (3.7–4.0)	<0.001
Congestive heart failure	33.1	18.8 (18.4–19.2)	29.9 (28.7–31.1)	16.9 (16.6–17.3)	<0.001
Stroke	7.1	3.3 (3.2–3.5)	4.7 (4.3–5.1)	3.1 (3.0–3.3)	<0.001
Dysrhythmia	25.9	13.6 (13.3–13.9)	20.9 (19.9–21.9)	11.0 (10.8–11.3)	<0.001
Any cardiovascular event	45.8	28.8 (28.3–29.3)	44.2 (42.7–45.8)	19.7 (19.3–20.0)	<0.001

* All deaths were assigned to one of the four broad groups of causes listed.
† The five most frequently reported individual causes of death are listed.

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CLINICAL RESEARCH www.jasn.org

High-Efficiency Postdilution Online Hemodiafiltration Reduces All-Cause Mortality in Hemodialysis Patients

Francisco Maduell,* Francesc Moreso,† Mercedes Pons,‡ Rosa Ramos,§ Josep Mora-Macià,‖ Jordi Carreras,¶ Jordi Soler,** Ferran Torres,††‡‡ Josep M. Campistol,* and Alberto Martinez-Castelao,§§ for the ESHOL Study Group

*Nephrology Department, Hospital Clinic, Barcelona, Spain; †Nephrology Department, Hospital Universitari Vall d'Hebron, Barcelona, Spain; ‡CETIRSA, Barcelona, Spain; §Hospital San Antonio Abad, Vilanova i la Geltru, Spain; ‖Fresenius Medical Care, Granollers, Spain; ¶Diaverum Baix Llobregat, L'Hospitalet, Llobregat, Spain; **Fresenius Medical Care, Reus, Spain; ††Biostatistics Unit, School of Medicine, Universitat Autònoma de Barcelona, Barcelona, Spain; ‡‡Biostatistics and Data Management Platform, IDIBAPS, Hospital Clinic, Barcelona, Spain; and §§Nephrology

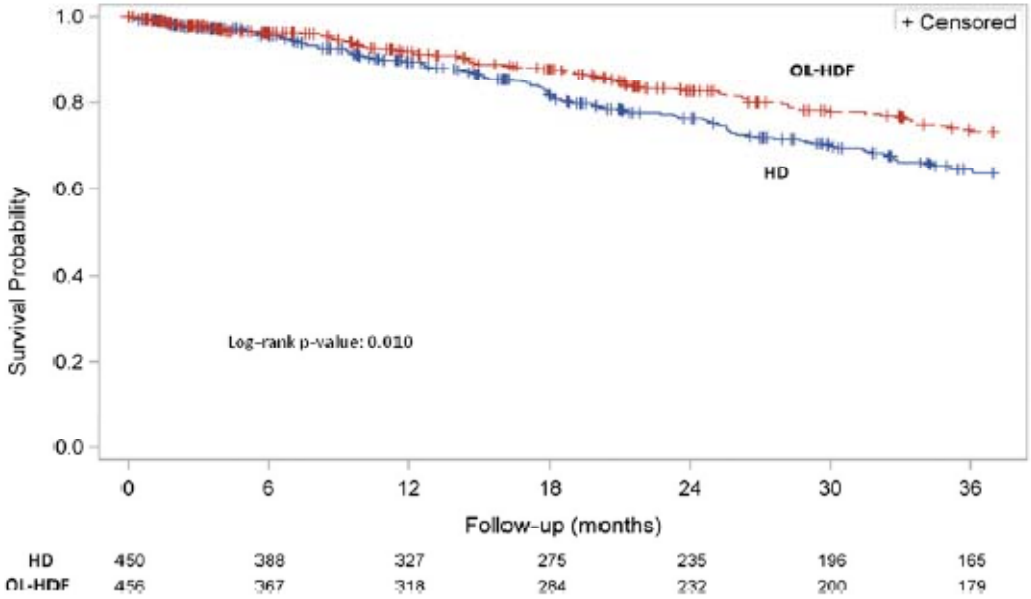

Figure 2. Kaplan–Meier curves for 36-month survival in the intention-to-treat population (P=0.01 by the log-rank test). HD, hemodialysis.

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mini review

http://www.kidney-international.org

Once upon a time in dialysis: the last days of Kt/*V*?

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When different thresholds of Kt/V_{urea} were compared in controlled trials, increasing its value above standard did not impact survival,[6,7] suggesting that the upper limit of improving outcomes based on this parameter had been reached. This

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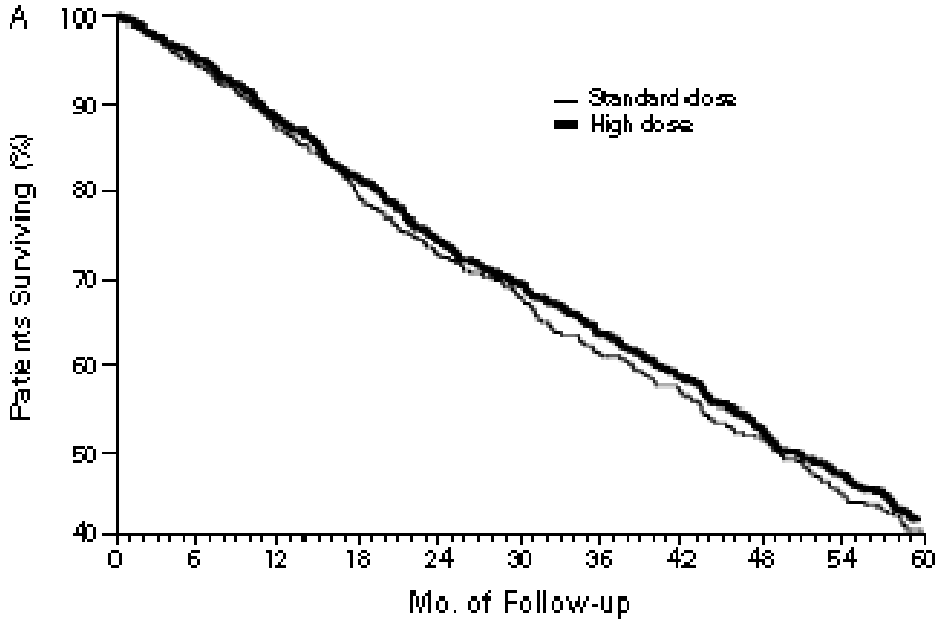
The New England Journal of Medicine

EFFECT OF DIALYSIS DOSE AND MEMBRANE FLUX IN MAINTENANCE HEMODIALYSIS

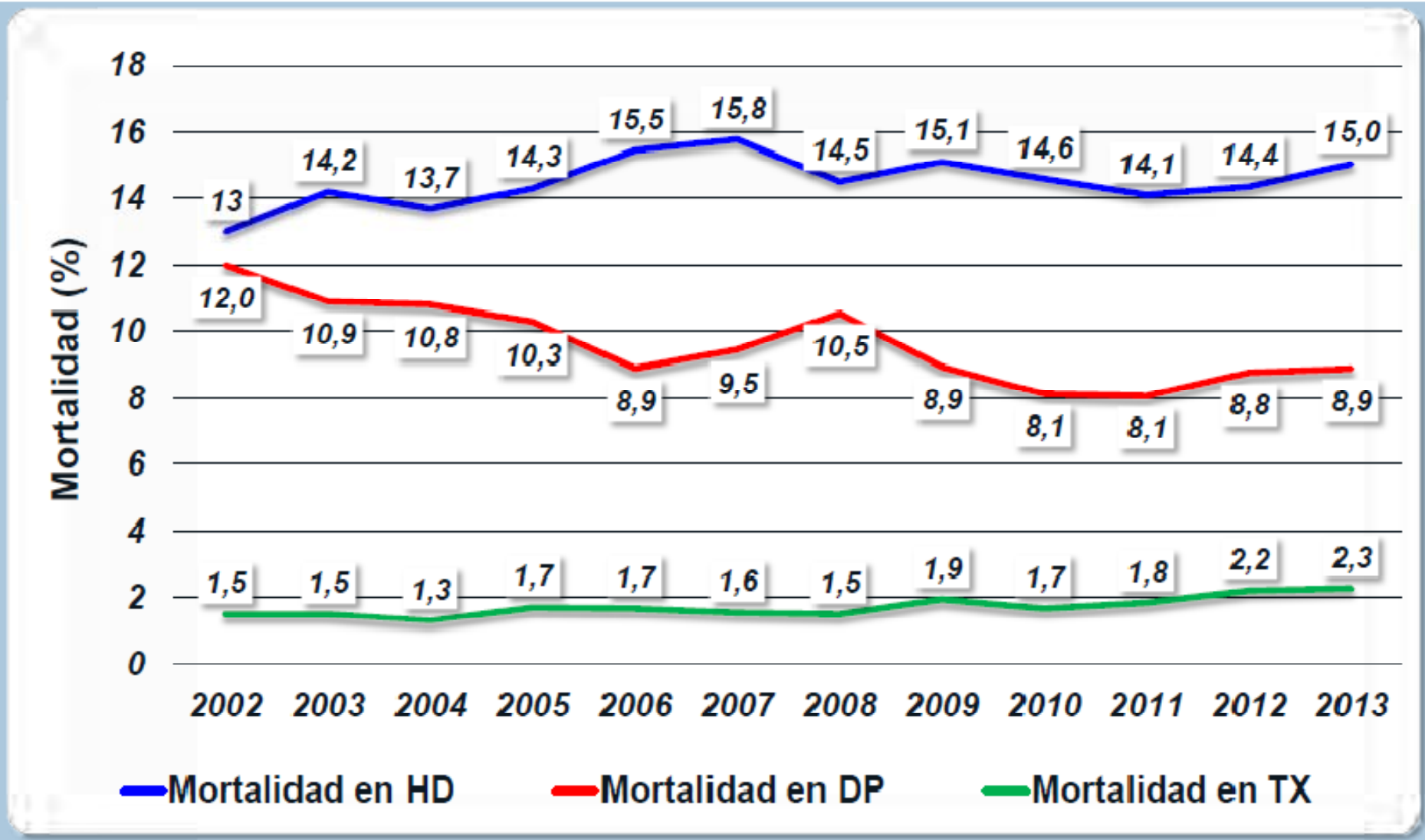
GARABED EKNOYAN, M.D., GERALD J. BECK, PH.D., ALFRED K. CHEUNG, M.D., JOHN T. DAUGIRDAS, M.D., TOM GREENE, PH.D., JOHN W. KUSEK, PH.D., MICHAEL ALLON, M.D., JAMES BAILEY, M.D., JAMES A. DELMEZ, M.D., THOMAS A. DEPNER, M.D., JOHANNA T. DWYER, D.SC., R.D., ANDREW S. LEVEY, M.D., NATHAN W. LEVIN, M.D., EDGAR MILFORD, M.D., DANIEL B. ORNT, M.D., MICHAEL V. ROCCO, M.D., GERALD SCHULMAN, M.D., STEVE J. SCHWAB, M.D., BRENDAN P. TEEHAN, M.D., AND ROBERT TOTO, M.D., FOR THE HEMODIALYSIS (HEMO) STUDY GROUP*



No. at Risk

Standard dose	854	759	680	524	451	382	315	253	197	149
High dose	857	753	687	538	470	389	327	266	219	166

Evolución de la Mortalidad



THE EVIDENCE OF THE TOXICITY OF UREA IS LIMITED

To the best of our knowledge, only a few experimental studies point to a toxic effect of urea at concentrations currently observed in uremia. D'Apolito *et al.*[10] found that urea induced the generation of Radical Oxygen Species (ROS) and insulin resistance *in vitro* and in mice. In an *in vitro* study, Vaziri *et al.*[11] showed disruption of the intestinal epithelial barrier function by derangement of tight junctions. Trécherel *et al.*[12] explored regulatory proteins of apoptosis and showed an upregulation of Bcl2-associated death promoter, a pro-apoptotic protein.

The clinical equivalent to these experimental suggestions is, however, scanty. Adding urea to the dialysate up to concentrations two to three times higher than usual in dialysis patients induced no consistent changes in uremic symptoms.[13] Increasing urea removal in controlled trials had no impact on hard clinical outcomes.[6,7] An observational study by Koeth *et al.*[14] found an association with mortality of homocitrulline, a marker of carbamylation to which also urea is supposed to contribute. However, the concentration of urea was only modestly correlated to that of homocitrulline, with an R^2 of 0.14, suggesting that other factors than urea were more important for homocitrulline generation and its association to death. In addition, urea by itself was not related to mortality.[14]

Thus, urea, in spite of its everyday application as marker of dialysis adequacy, has rarely been assessed for its toxicity and up till now has not been proven in clinical studies to affect outcomes. Its choice as a marker cannot really be supported by robust biochemical or clinical arguments. However, even if urea would be a recognized toxin, there remain questions about the representativeness of Kt/V_{urea} for the removal of other uremic retention solutes.

Evaluating a new method to judge dialysis treatment using online measurements of ionic clearance

EG Lowrie[1], Z Li[1], NJ Ofsthun[1] and JM Lazarus[1]

[1]*Fresenius Medical Care (North America), Lexington, Massachusetts, USA*

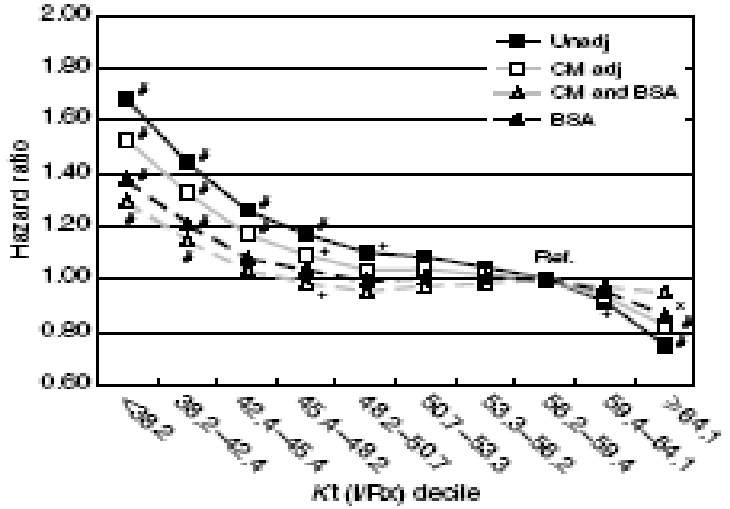


Figure 2 | Risk profiles for *Kt*. Four levels of statistical adjustment are shown: unadjusted (Unadj: ■), case mix adjusted (CM Adj: □), case mix and BSA adjusted (CM and BSA: △), and BSA adjusted (BSA: ▲). The hazard ratios are compared to a common reference decile (Ref) for each analysis and the probability that each ratio is not different from its reference value is shown by a symbol near the ratio: $^{\#}P<0.01$, $^{\times}P<0.05$, and $^{+}P<0.10$. No symbol means not different ($P>0.10$).

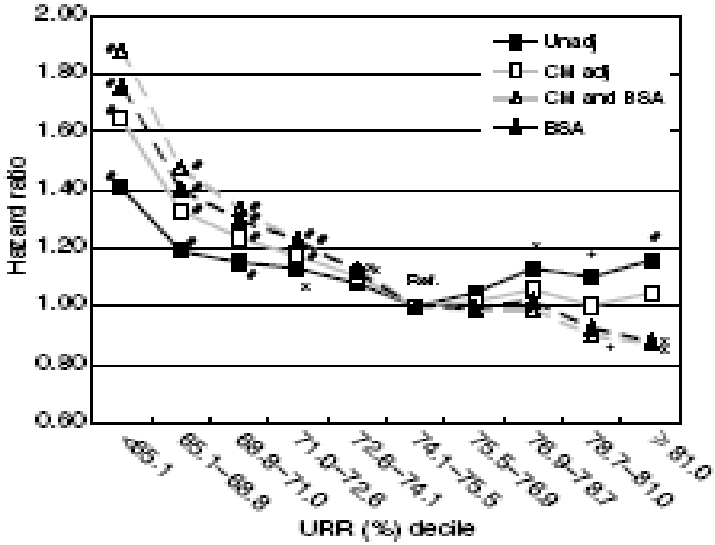


Figure 3 | Risk profiles for the URR. Four levels of statistical adjustment are shown: unadjusted (Unadj: ■), case mix adjusted (CM Adj: □), case mix and BSA adjusted (CM and BSA: △), and BSA adjusted (BSA: ▲). The hazard ratios are compared to a common reference decile (Ref) for each analysis and the probability that each ratio is not different from its reference value is shown by a symbol near the ratio: $^{\#}P<0.01$, $^{\times}P<0.05$, and $^{+}P<0.10$. No symbol means not different ($P>0.10$).

http://www.kidney-international.org original article

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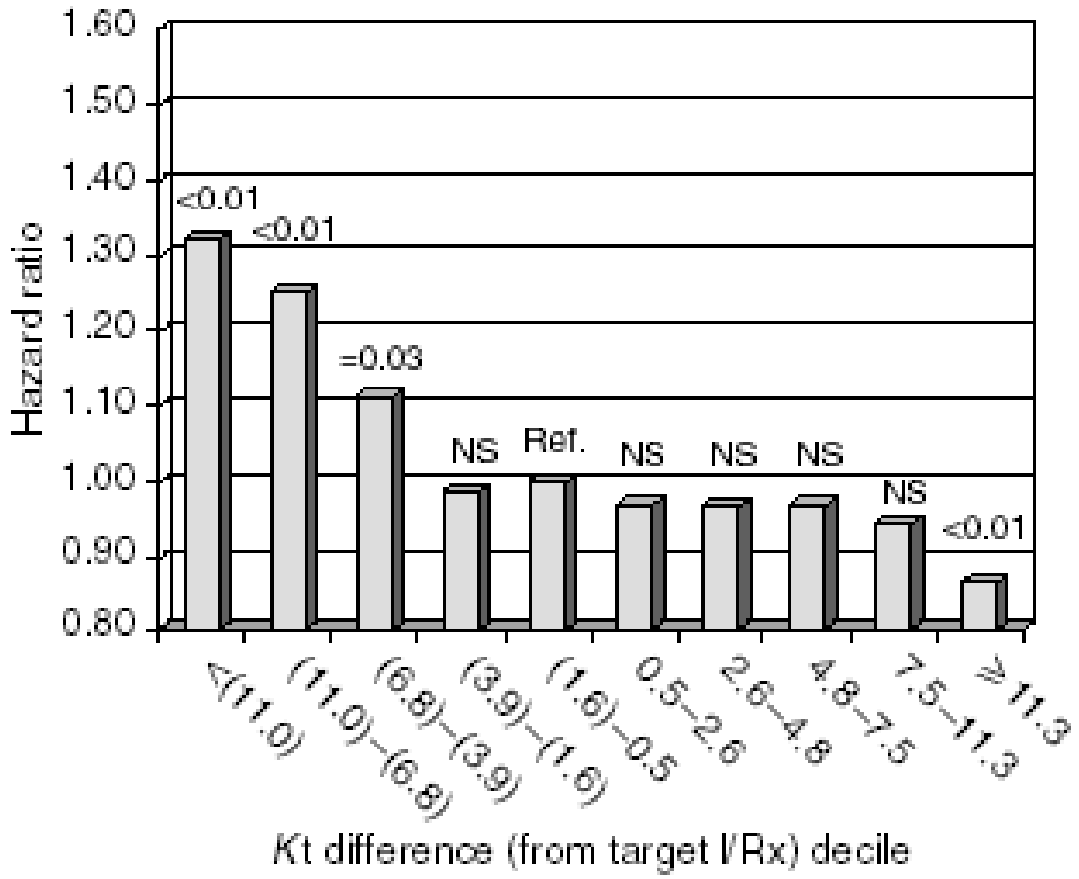


http://www.senefro.org

Kt como control y seguimiento de la dosis en una unidad de hemodiálisis

F. Maduell, M. Vera, N. Serra, S. Collado, M. Carrera, A. Fernández, M. Arias, M. Blasco, E. Bergadá, A. Cases y J. M.ª Campistol

Servicio de Nefrología. Hospital Clínic Barcelona.

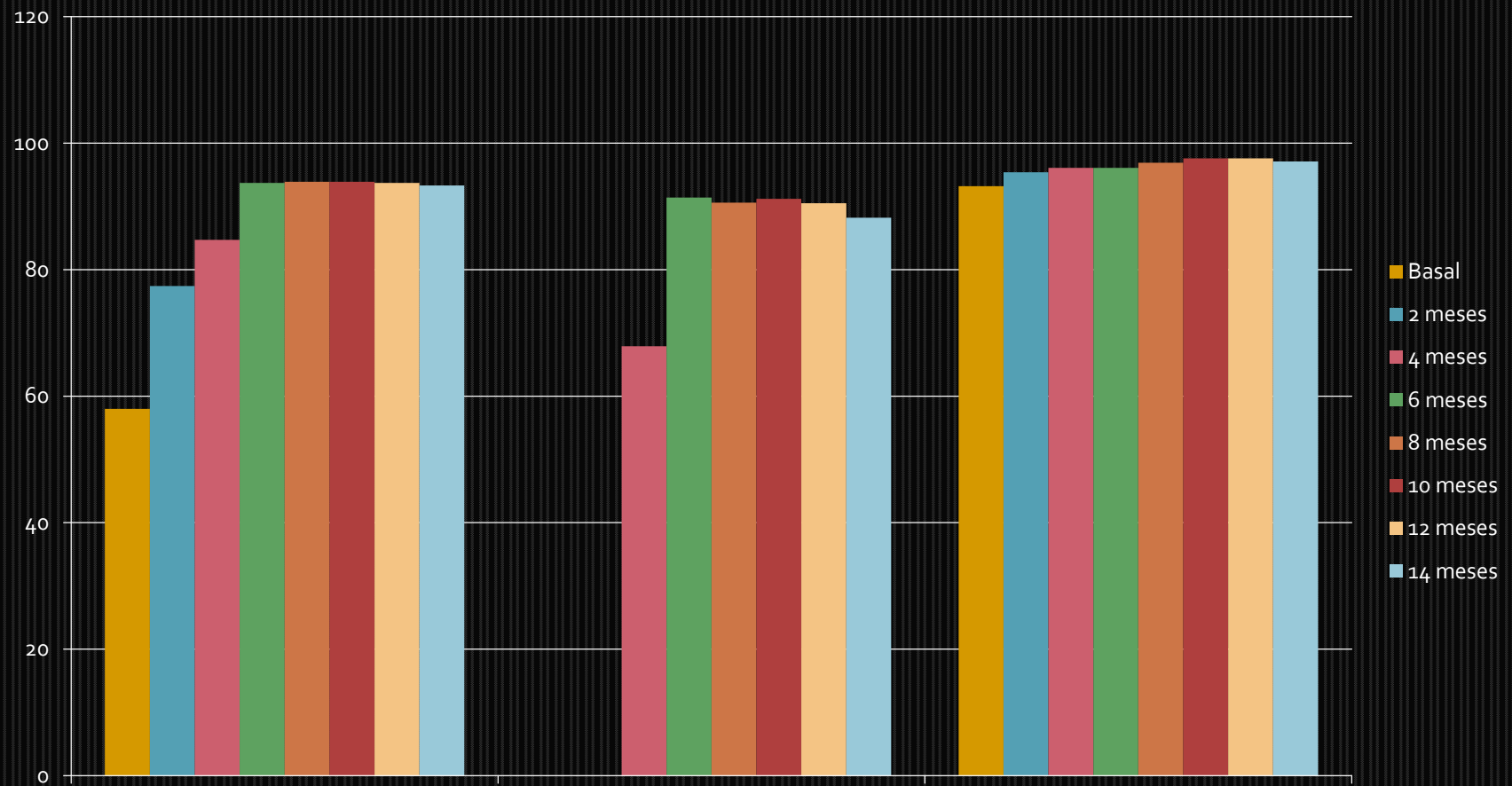
Nefrología 2008; 28 (1) 43-47

Tabla II. Diferencias entre la dosis prescrita y la alcanzada según las diferentes recomendaciones

	Dosis prescrita	Dosis alcanzada	Pacientes cumplen	% de pacientes que cumplen
Kt/V > 1,3	1,3	1,98 ± 0,5	51	100%
PRU > 70%	70	79,2 ± 7	46	90%
Kt > 45 L	45	56,6 ± 14	40	78%
Kt Mujeres > 45L Hombres > 50L	48,1 ± 2	53,4 ± 12 58,5 ± 14	35	69%
Kt según ASC	49,1 ± 4	56.6 ± 14	29	57%

mínima prescrita, con 4,6 ± 3,4 L menos de dosis. Concluimos que el seguimiento de la dosis de diálisis con el Kt, permite una mejor discriminación de la adecuación de diálisis, identificando entre el 30 y el 40% de pacientes que quizá no alcanzasen una dosis adecuada para su género o para su superficie corporal.

Kt como indicador de calidad en el área de prescripción en hemodiálisis



M. Molina y cols. Nefrología 2010;30(3):331-336

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ORIGINAL ARTICLE

Impact of targeting *Kt* instead of *Kt/V*

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Keywords: adequacy, dialysis dose, ionic dialysance, *Kt*, online monitoring

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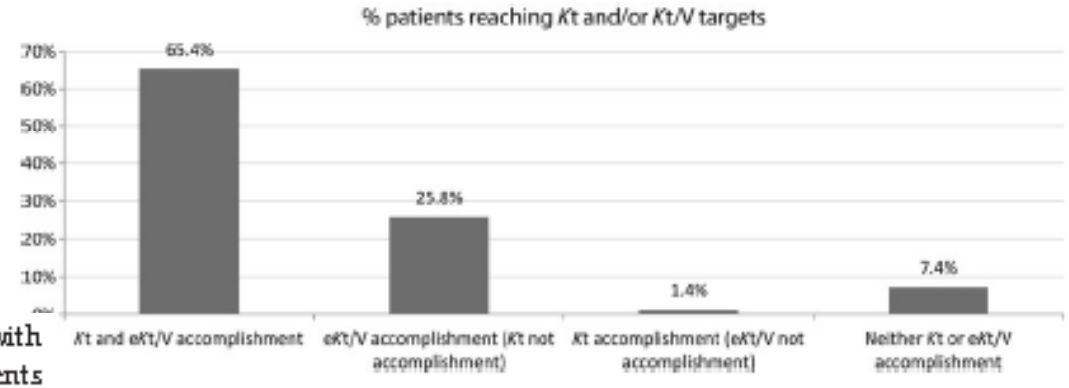

FIGURE 1: Percentage of patients achieving the minimum prescribed *eKt/V* and/or *Kt* (*n* = 3275).

In conclusion, the advantage of monitoring the dose with *Kt* instead *Kt/V* is that this method identifies 25.8% of patients who did not reach the minimum *Kt* while achieving *Kt/V*. This difference is particularly evident in women, in patients with a low body weight, and in those with venous central catheters. The routine use of *Kt* is recommended in all patients who are routinely dialyzed with HD monitors. Although there is still a lack of scientific evidence on the use of *Kt*, now seems the right time to prepare for a change. The percentage of HD machines providing *Kt* has increased in the last few years and could probably reach nearly 100% in the next few years. Therefore, the time is ripe for studies such as our own to rethink dose monitoring and for prospective studies to define and validate the minimum *Kt* recommendations.

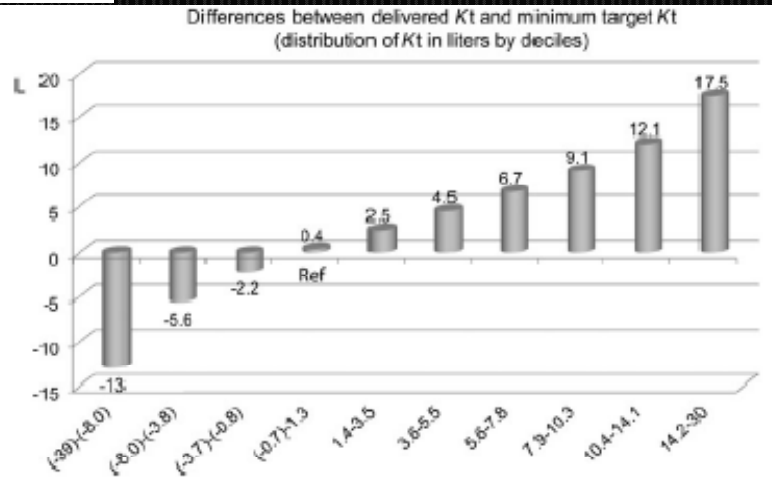

FIGURE 2: Differences between the *Kt* administered and the minimum prescribed *Kt* (distribution by deciles of liters of *Kt* received; *n* = 3275).

kidney INTERNATIONAL ISN

Adequate Kt Dose: A Prospective, Non-interventional, Multicenter Study to Evaluate Mortality and Hospitalization Risk

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Manuscript ID	KI-03-16-0463.R3
Article Type:	Clinical Investigation
Date Submitted by the Author:	05-Aug-2016
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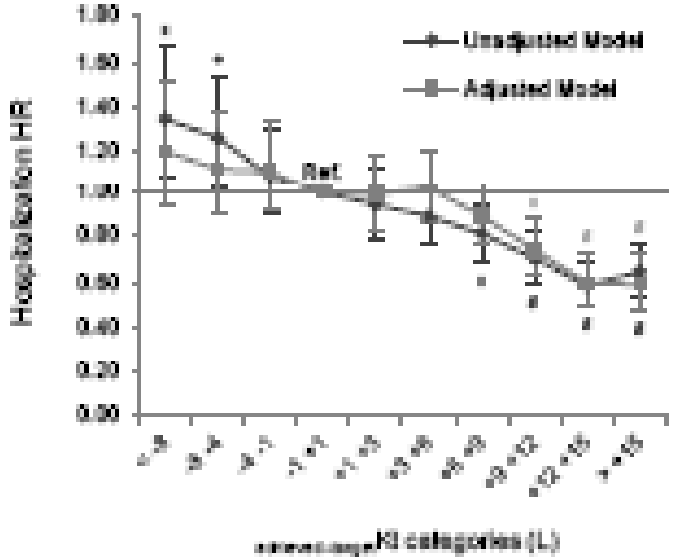

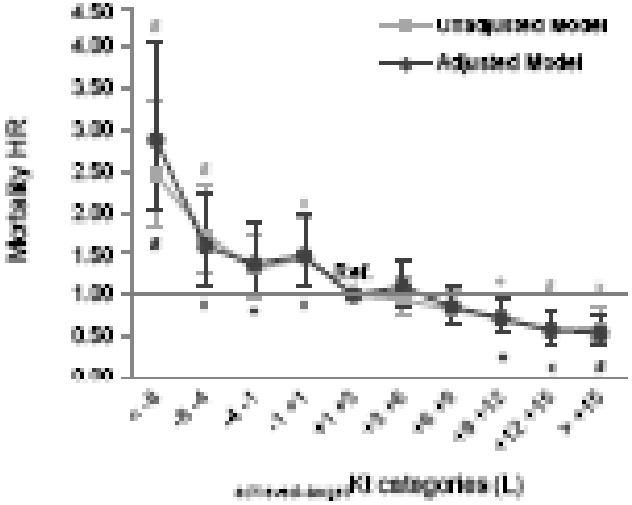

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In conclusion, current recommendations for monitoring the dialysis dose with Kt individualized for BSA have been validated in this prospective study in the current Spanish dialysis population, and the dose is predictably associated with death and hospitalization risk. Prescribing an additional 3 L or more of the current Kt individualized for BSA could reduce the risk of mortality, and an additional 9 L or more could reduce the risk of hospitalization.

CLINICAL RESEARCH www.jasn.org

High-Efficiency Postdilution Online Hemodiafiltration Reduces All-Cause Mortality in Hemodialysis Patients

Francisco Maduell,* Francesc Moreso,† Mercedes Pons,‡ Rosa Ramos,§ Josep Mora-Macià,‖ Jordi Carreras,¶ Jordi Soler,** Ferran Torres,††‡‡ Josep M. Campistol,* and Alberto Martinez-Castelao,§§ for the ESHOL Study Group

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other uremic retention solutes.

THE KINETICS OF UREA ARE NOT REPRESENTATIVE FOR OTHER SOLUTES, OF WHICH TOXICITY IS BETTER DOCUMENTED

Basic principles of kinetic modeling

(Figures 1 and 2) The concept of dialysis kinetic analysis lays at the origin of urea kinetic modeling.[15] The basic principle is the mirror image of pharmacokinetics, where the distribution pattern of a drug throughout the body to reach the most remote compartments is studied after the plasma concentration rises

Small water soluble compounds

The question has been raised whether urea as one of the small water soluble compounds would have similar kinetics as other solutes with the same characteristics, such as the guanidino compounds, which have a well-documented biologic (toxic) impact.[18] However, when their kinetics were compared, distribution volume was definitely different and mostly larger for the guanidino compounds as compared with urea, giving rise to less efficient removal.[19] Those mathematical findings were corroborated by assessing *in vivo* concentrations of guanidino compounds in erythrocytes, the most easily

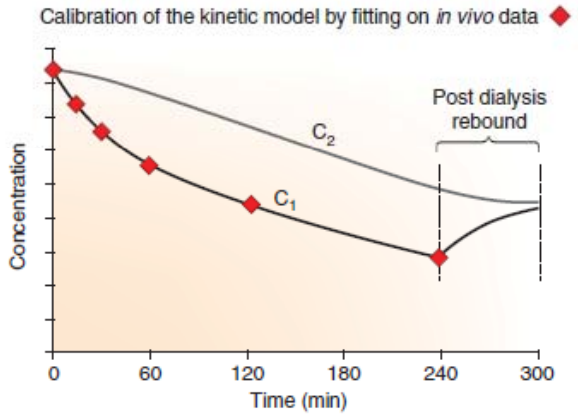

Figure 2 | Graphic illustration of the changes in solute concentration during dialysis that are reflected by kinetic studies. The diamonds illustrate real-life *in vivo* measurements of solute

bound toxins. In a study comparing high-flux hemodialysis with peritoneal dialysis, hemodialysis was more efficient for the removal of both urea and p-cresol, a surrogate for the sum of p-cresol conjugates.[26] However, this better removal by hemodialysis was translated only in lower circulating concentrations for urea. For p-cresol, in contrast, the concentration was lower with peritoneal dialysis, exactly opposite to what could be expected from the clearance values.[26] This discrepancy was confirmed in at least one other study[27] and suggests that, apart from removal adequacy, solute concentration in dialysis patients may be the consequence of other, non-dialysis phenomena;[28] those are unlikely to be grasped entirely by Kt/V_{urea}, a simple formula assessing the kinetic pattern of one single molecule.

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Osteocalcin and Myoglobin Removal in On-Line Hemodiafiltration Versus Low- and High-Flux Hemodialysis

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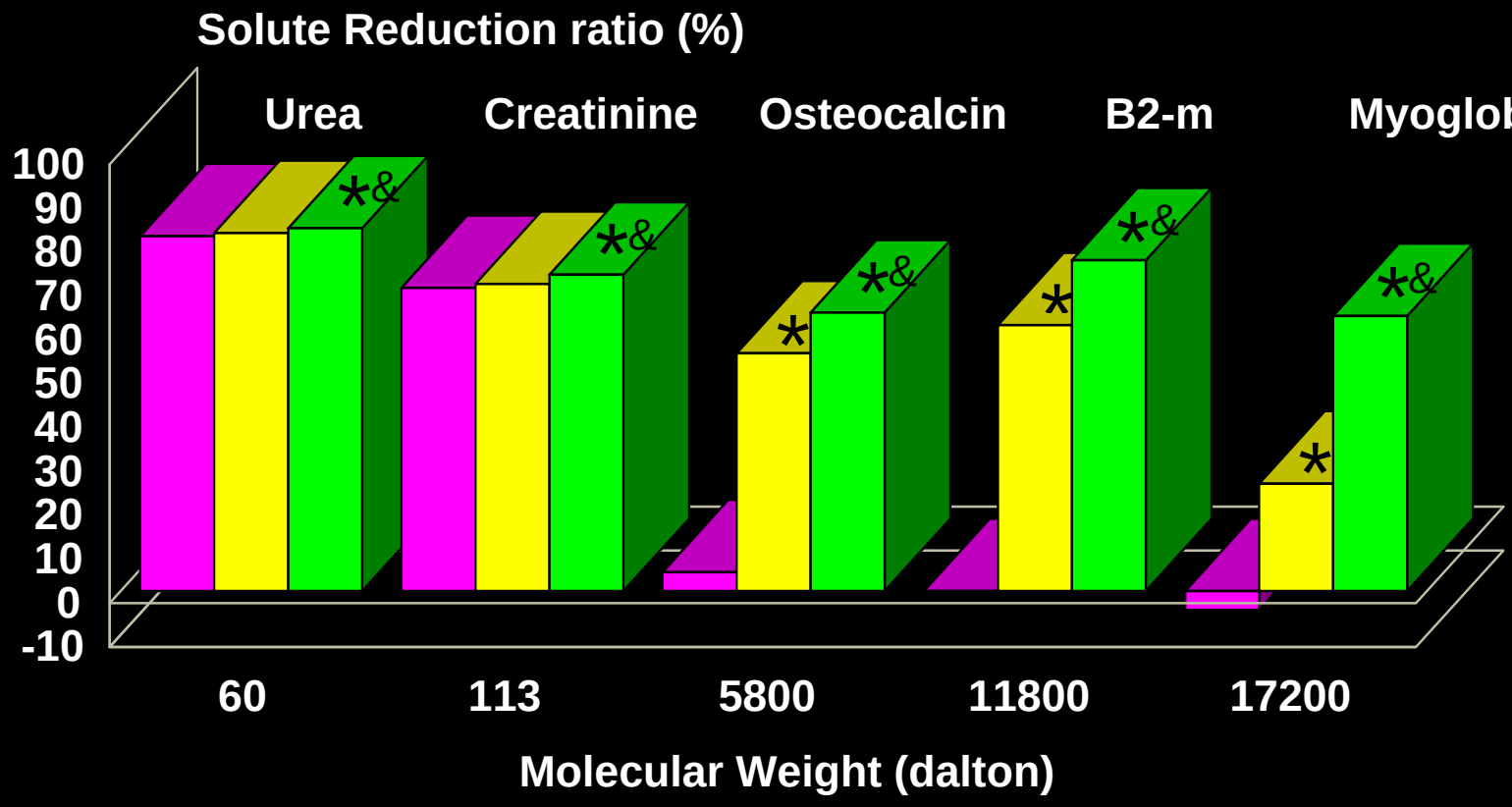
American Journal of Kidney Diseases, Vol 40, No 3 (September), 2002: pp 582-589



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doi: 10.1093/ndt/gfn521
Advance Access publication 17 September 2008

Original Article

NDT
Nephrology Dialysis Transplantation

Serum β_2-microglobulin level is a significant predictor of mortality in maintenance haemodialysis patients

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Conclusion. These results demonstrate that the serum β_2-M level is a significant predictor of mortality in haemodialysis patients, independent of haemodialysis duration, diabetes, malnutrition and chronic inflammation, suggesting the clinical importance of lowering serum β_2-M in these patients.

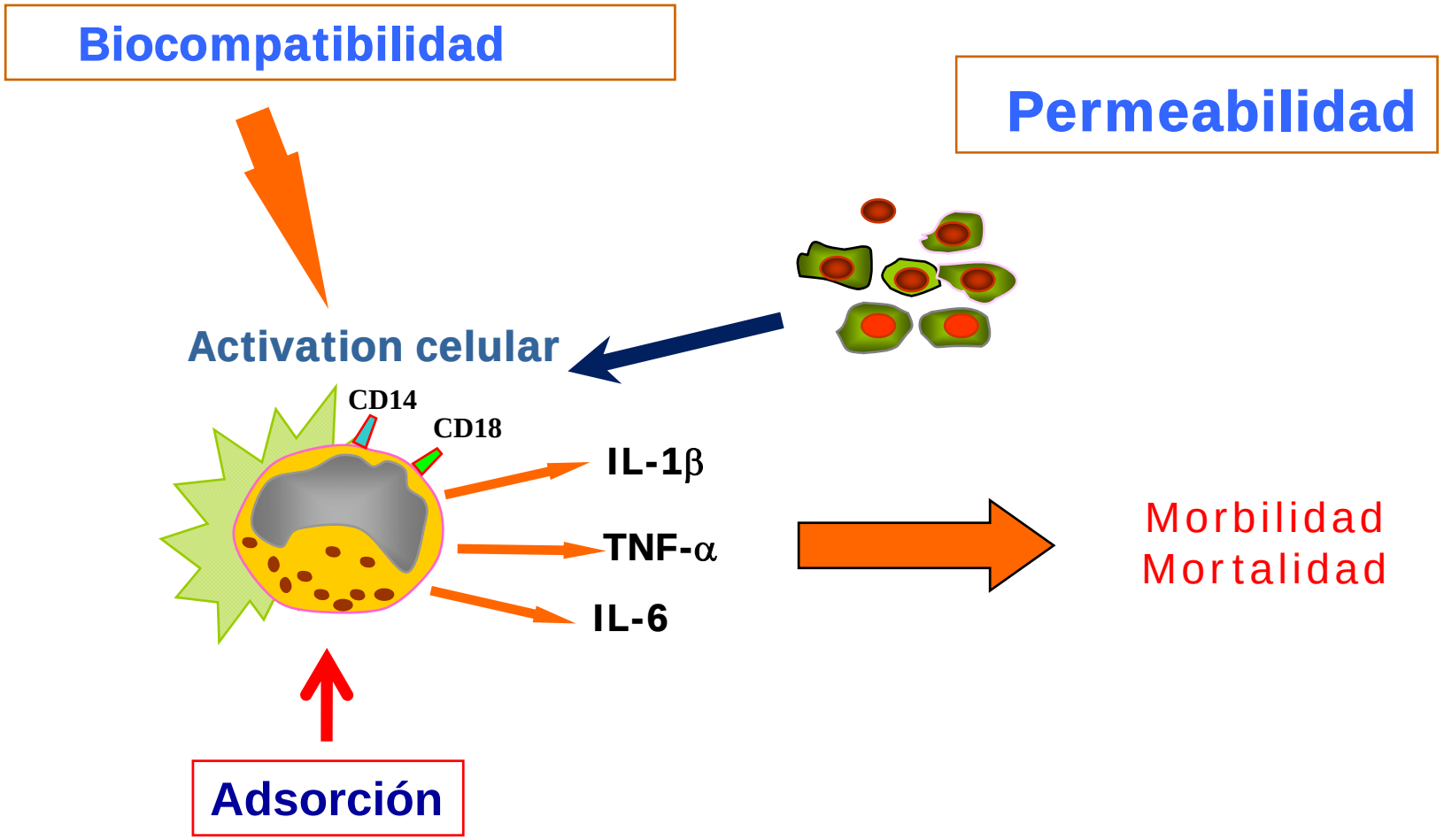
Association between Serum β_2-Microglobulin Level and Infectious Mortality in Hemodialysis Patients

Alfred K. Cheung,*† Tom Greene,† John K. Leypoldt,†‡ Guofen Yan,§ Michael Allon,‖ James Delmez,¶ Andrew S. Levey,** Nathan W. Levin,†† Michael V. Rocco,‡‡ Gerald Schulman,§§ and Garabed Eknoyan‖‖ for HEMO Study Group

Clin J Am Soc Nephrol 3: 69–77, 2008. doi: 10.2215/CJN.02340607

Conclusions: These results generally support the notion that middle molecules are associated with systemic toxicity and that their accumulation predisposes dialysis patients to infectious deaths, independent of the duration of maintenance dialysis.

Efecto de la membrana de HD



Kidney International, Vol. 58, Suppl. 76 (2000), pp. S-19–S-27

Confounding factors in the assessment of delivered hemodialysis dose

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Confounding factors in the assessment of delivered hemodialysis dose. A satisfactory dialysis patient's outcome results from an effective and personalized therapy. However, the higher the prescribed efficiency, the more likely it is that the prescribed dose is incorrectly administered. Avoiding discrepancies between the prescribed and delivered doses calls for a continuous surveillance, from urea kinetics to urea biosensors. An unexpectedly low efficiency result may affect several patients or may just be limited to the individual patient. An inadequate calibration of blood and dialysate pumps or manufacturing defects in blood tubings or needles may be responsible for a more diffuse phenomenon. The most frequently detected factors in the individual patient are poor vascular access, recirculation, decreases in dialyzer performance and insufficient anticoagulation. However, urea removal per se is not enough to satisfy all the assumptions underlying an adequate dialysis therapy. Indeed, dialysis adequacy is achieved by way of a complex combination of numerous elements transcending urea removal alone: acidosis correction, the achievement of dry body weight, fluid and electrolyte homeostasis, good blood pressure control, overall biocompatibility, anemia and malnutrition correction, and finally, a customized schedule together with treatment duration.

The question of what actually constitutes adequate dialysis for uremic patients is a controversial and debated issue within the dialysis community [1–4].

The first point in discussing dialysis adequacy concerns physiological role. The toxicity might be due to the synergism of specific toxic effects when several components are brought together. However, the absence of any reliable and universally acceptable markers has prevented the standardization of dialysis therapy until urea was elected as a marker of patient outcome [6]. This choice has been ratified by the National Cooperative Dialysis Study [7], which assessed the role of the blood urea nitrogen concentration along with the length of the dialysis session as parameters of the adequacy in long-term dialysis therapy. Nowadays, some evidence has confirmed these early insights, and it has been suggested that the dialysis patient's outcome may be related to dialysis dose and nutritional status [8].

In terms of dialysis dose, the response is usually monitored by means of urea kinetic modeling (UKM) and efficiency-related quantities: (*1*) The Qt, calculated as a product of the blood flow rate and the treatment time, represents the total blood volume cleared during the dialysis session. (*2*) The Kt, a product of instantaneous clearance and treatment time, indicates the absolute depuration achieved during the treatment. (*3*) The Kt/V is a dimensionless index reflecting how the achieved depuration is adapted to the individual patient, with V being

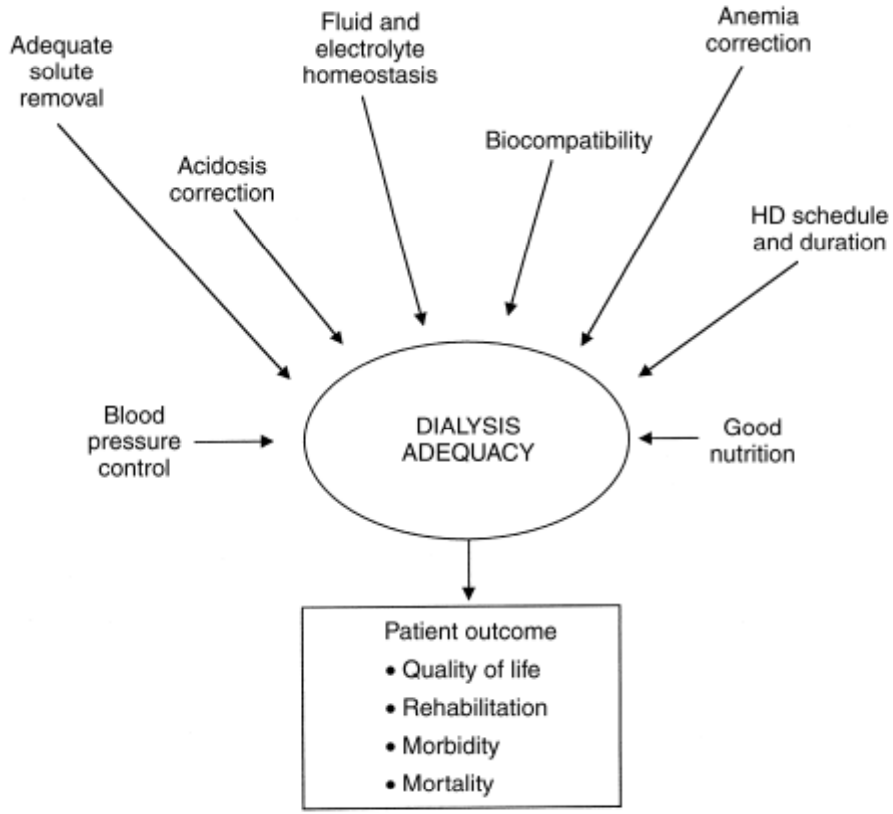

Fig. 7. Determinants of dialysis adequacy.