Emodialisi vs emodiafiltrazione

VINCENZO PANICHI

Nephrol Dial Transplant (2019) 1–10
doi: 10.1093/ndt/gfz005

ndt
Nephrology Dialysis Transplantation

Global prevalent use, trends and practices in haemodiafiltration

Bernard Canaud[1,2], Katrin Köhler[1], Jan-Michael Sichart[3] and Stefan Möller[3]

In brief, haemodialysis has moved from:

In brief, haemodialysis has moved from:

Long dialysis	**Short dialysis**	**1975**
Uncontrolled	**Controlled ultrafiltration**	**1978**
Acetate	**Bicarbonate**	**1978-1983**
Bioincompatible	**Biocompatible**	**1993**
Low flux	**High flux**	**2002-2003**
Contaminated	**Ultrapure dialysis fluid**	**2011-2012,**

…and finally from purely diffusive focusing on small uraemic toxins to enhanced convective modalities (e.g. online haemodiafiltration, HDF) enlarging the spectrum of compounds removed to middle and larger uraemic toxins .

Classification of uremic toxins

European Uremic Toxin Work Group of the ESAO

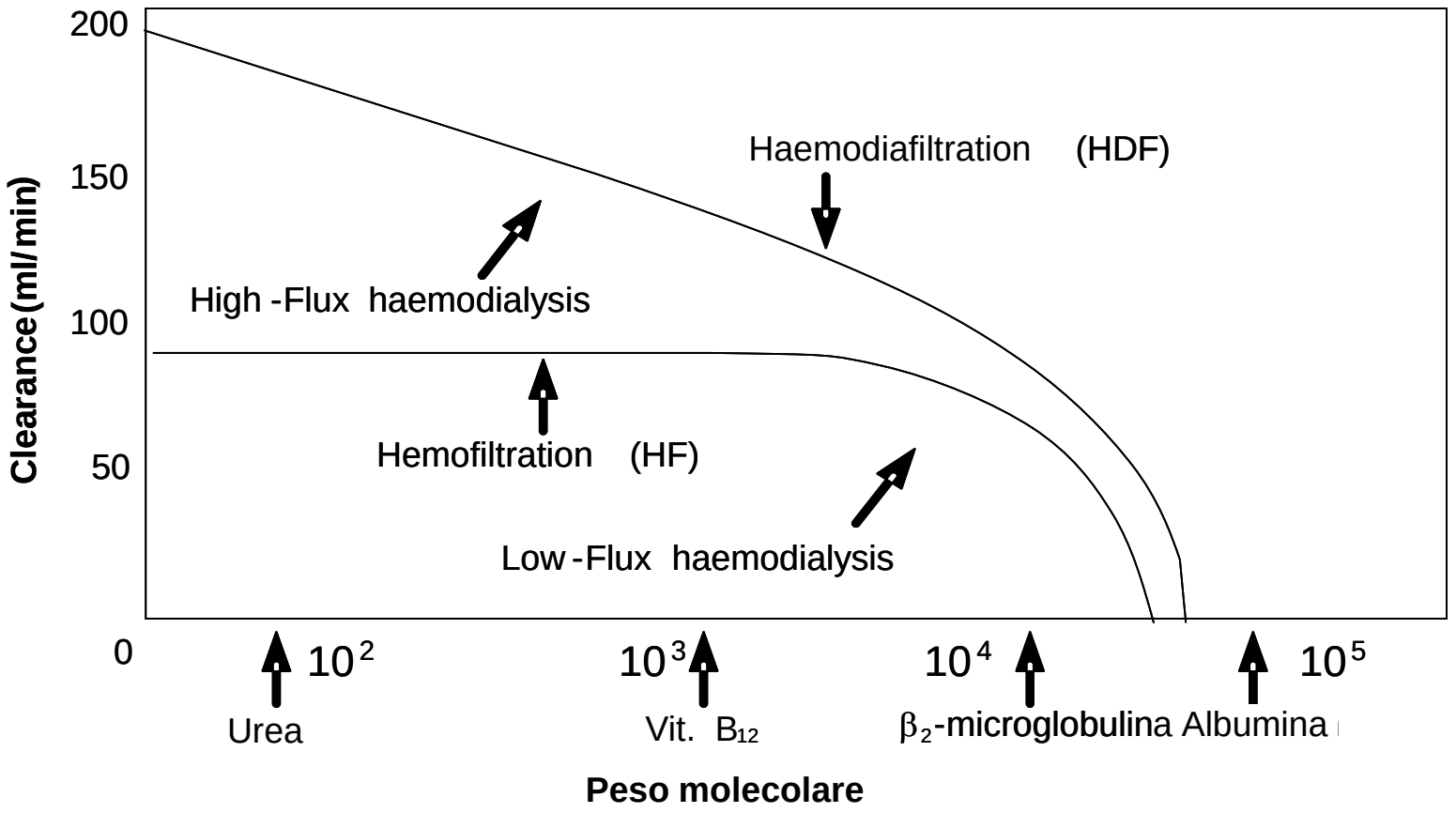
Small water soluble solutes	Protein-bound solutes	Middle molecu
Asymmetric dimethylarginine	3-Deoxyglucosone	Adrenomedullin
Benzylalcohol	CMPF*	Atrial natriuretic peptide
ß-Guanidinopropionic acid	Fructoselysine	$ß_2$-Microglobulin
ß-Lipotropin	Glyoxal	ß-Endorphin
Creatinine	Hippuric acid	Cholecystokinin
Cytidine	Homocysteine	Clara cell protein
Guanidine	Hydroquinone	Complement factor D
Guanidinoacetic acid	Indole-3-acetic acid	Cystatin C
Guanidinosuccinic acid	Indoxyl sulfate	Degranulation inhibiting protein I
Hypoxanthine	Kinurenine	Delta-sleep-inducing peptide
Malondialdehyde	Kynurenic acid	Endothelin
Methylguanidine	Methylglyoxal	Hyaluronic acid
Myoinositol	N-carboxymethyllysine	Interleukin 1ß
Orotic acid	P-cresol	Interleukin 6
Orotidine	Pentosidine	Kappa-Ig light chain
Oxalate	Phenol	Lambda-Ig light chain
Pseudouridine	P-OHhippuric acid	Leptin
Symmetric dimethylarginine	Quinolinic acid	Methionine-enkepahlin
Urea	Spermidine	Neuropeptide Y
Uric acid	Spermine	Parathyroid hormone
Xanthine		Retinol binding protein
		Tumor necrosis factor alpha

*CMPF is carboxy-methyl-propyl-furanpropionic acid

SIN RENI SOCIETÀ ITALIANA NEFROLOGIA

Vanholder R. et al New insights in uremic toxins. *Kidney Int*, 2003, 63; 84: S6–S10

Clearance e peso molecolare in diverse tecniche dialitiche



Online HDF in the World

~ 26%

~ 11%

Virtually 0%

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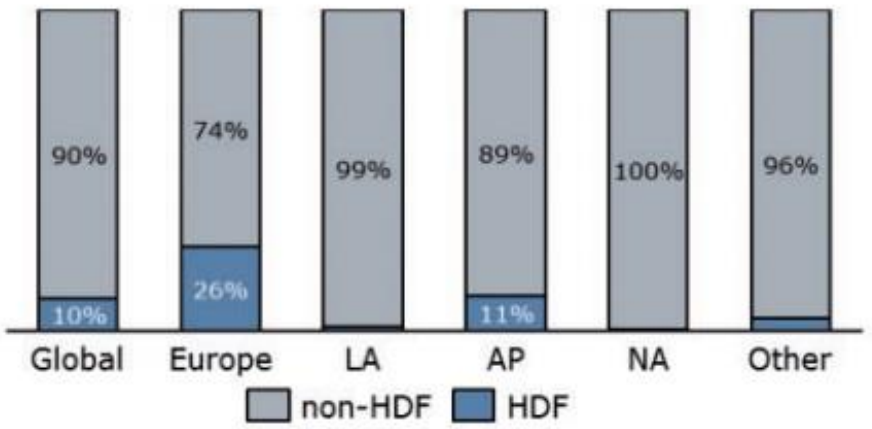
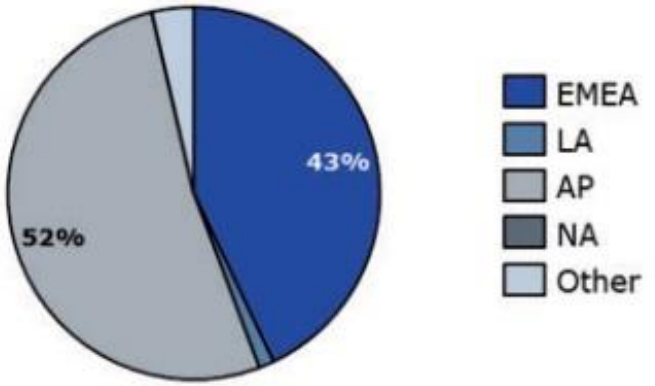
Regional Share of HDF Patients



Regional Distribution of HDF Patients



Abbreviation: LA: Latin America; AP: Asia Pacific; NA: North America.

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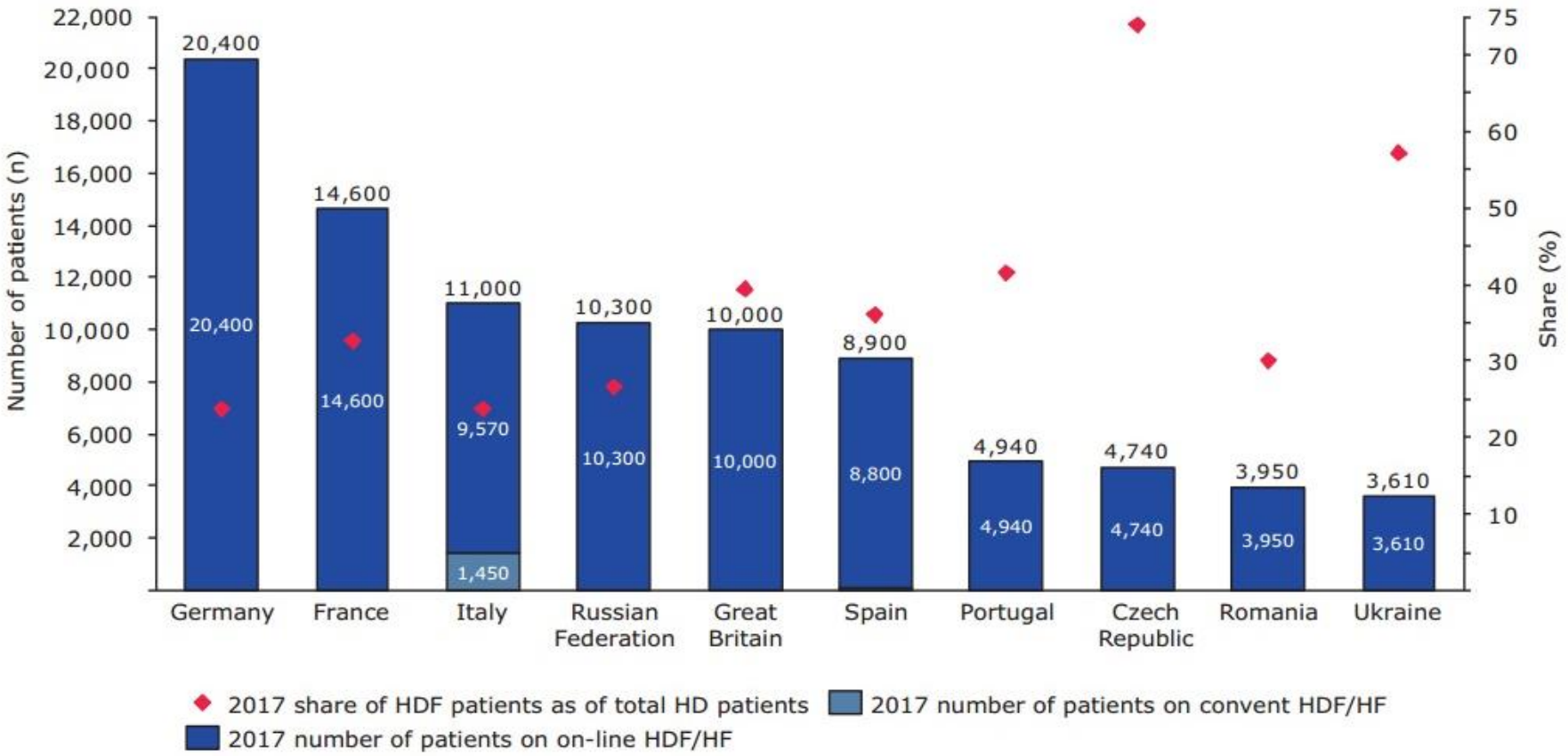
Europe HDF Patient Population



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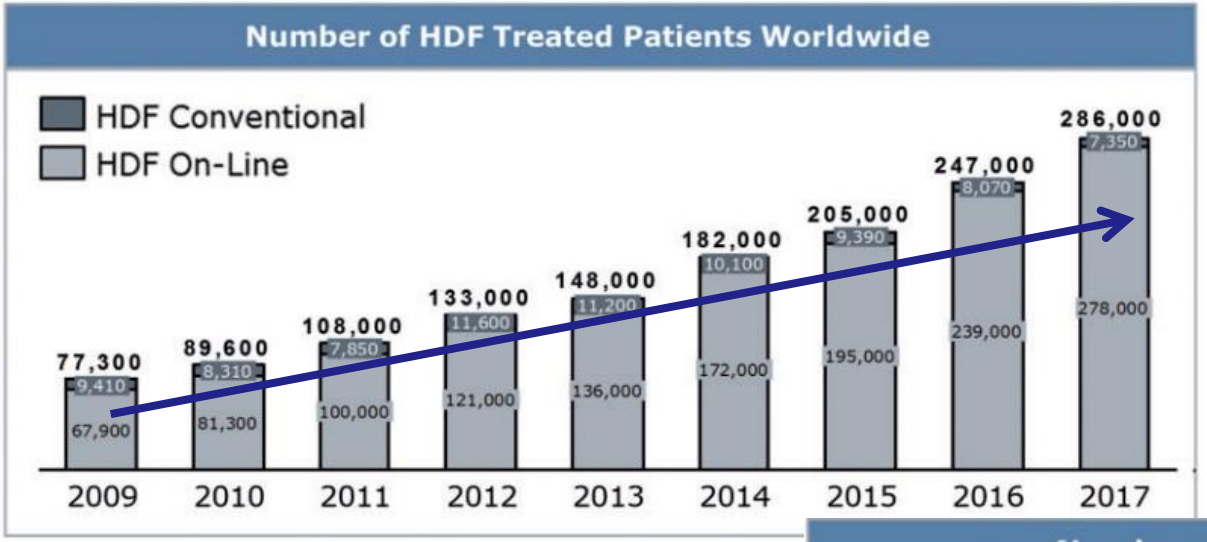
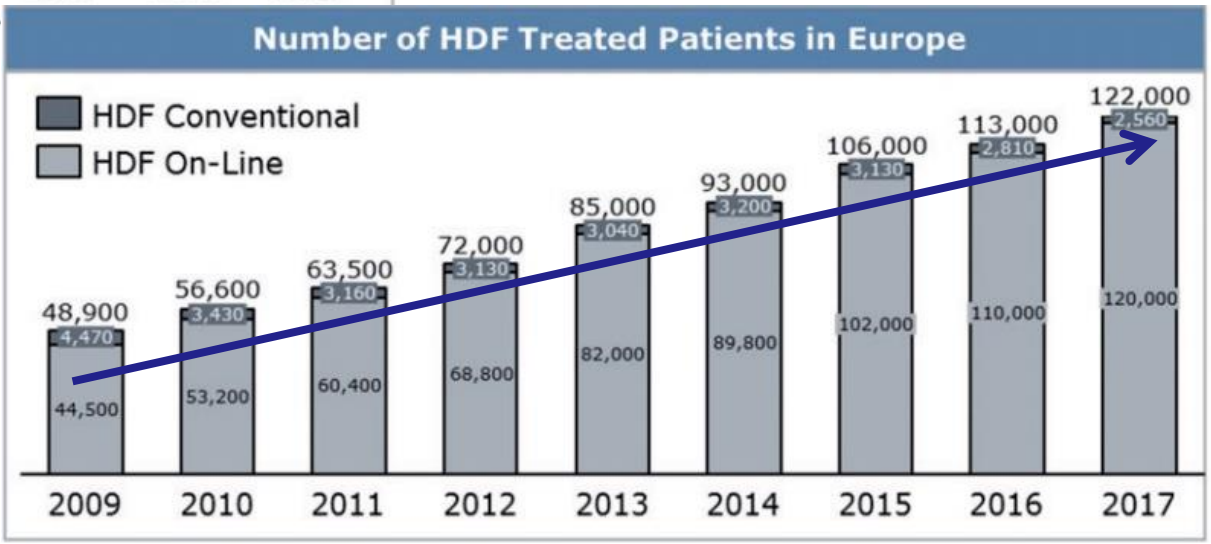
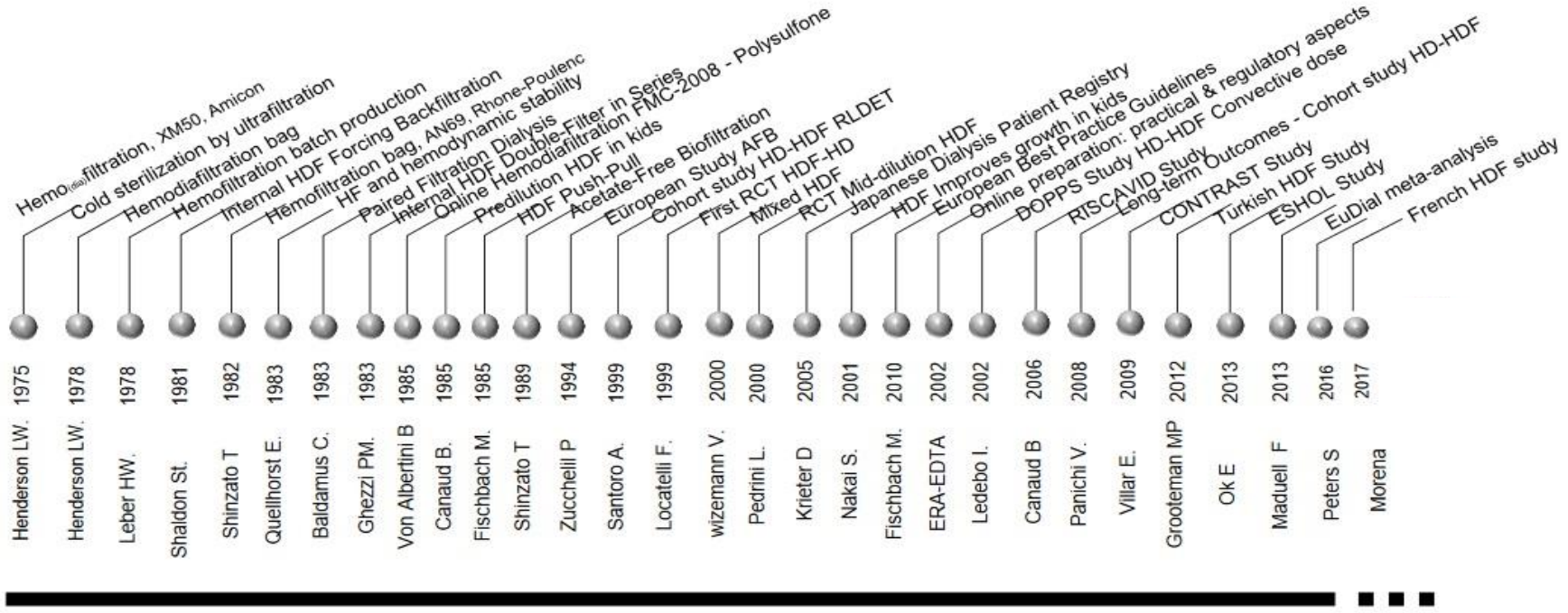
WORLD



EUROPE



Major milestones in online HDF development



Adapted from figure by Bernard Canaud

UMC Utrecht
Center for Circulatory Health

FRENCH HDF STUDY **391** PATIENTS 2004

TURKISH HDF **782** PATIENTS 2013

CONTRAST STUDY

714 PATIENTS

2012

ESHOL **906** PATIENTS **2013**

Randomized clinical trials in Europe evaluating HDF vs HD

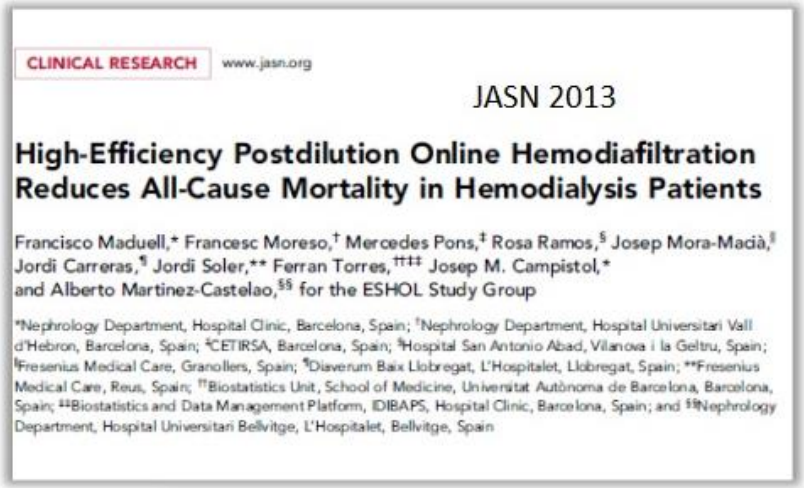
CLINICAL RESEARCH www.jasn.org

JASN 2012

Effect of Online Hemodiafiltration on All-Cause Mortality and Cardiovascular Outcomes

Muriel P.C. Grooteman,*† Marinus A. van den Dorpel,‡ Michiel L. Bots,§ E. Lars Penne,*‖ Neelke C. van der Weerd,* Albert H.A. Mazairac,‖ Claire H. den Hoedt,‡‖ Ingeborg van der Tweel,§ Renée Lévesque,¶ Menso J. Nubé,*† Piet M. ter Wee,*† and Peter J. Blankestijn,‖ for the CONTRAST Investigators

*Department of Nephrology, VU University Medical Center, Amsterdam, The Netherlands; †Institute for Cardiovascular Research, VU Medical Center, Amsterdam, The Netherlands; ‡Department of Internal Medicine, Maasstad Hospital, Rotterdam, The Netherlands; §Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, The Netherlands; ‖Department of Nephrology, University Medical Center Utrecht, Utrecht, The Netherlands; and ¶Department of Nephrology, Centre Hospitalier de l'Université de Montréal, St. Luc Hospital, Montréal, Canada



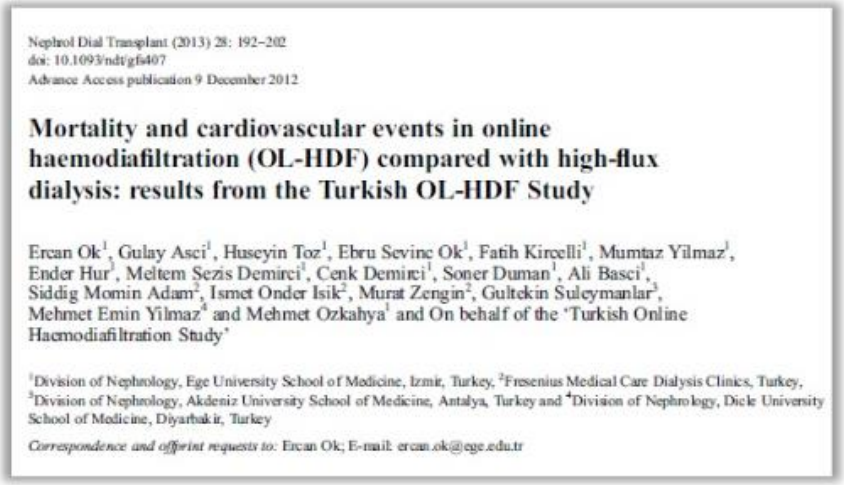
CLINICAL RESEARCH www.jasn.org

JASN 2013

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 Department, Hospital Universitari Bellvitge, L'Hospitalet, Bellvitge, Spain



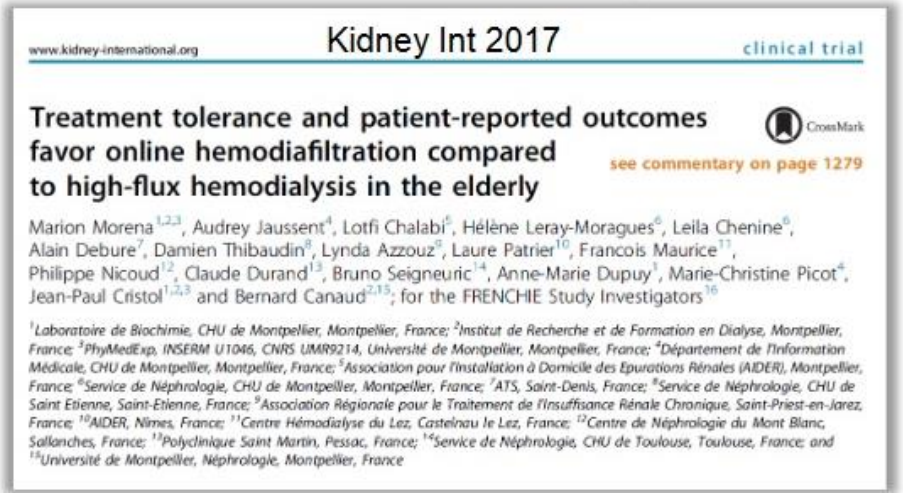
Nephrol Dial Transplant (2013) 28: 192–202
doi: 10.1093/ndt/gfs407
Advance Access publication 9 December 2012

Mortality and cardiovascular events in online haemodiafiltration (OL-HDF) compared with high-flux dialysis: results from the Turkish OL-HDF Study

Ercan Ok[1], Gulay Asci[1], Huseyin Toz[1], Ebru Sevinc Ok[1], Fatih Kircelli[1], Mumtaz Yilmaz[1], Ender Hur[1], Meltem Sezis Demirci[1], Cenk Demirci[1], Soner Duman[1], Ali Basci[1], Siddig Momin Adam[2], Ismet Onder Isik[2], Murat Zengin[2], Gultekin Suleymanlar[3], Mehmet Emin Yilmaz[4] and Mehmet Ozkahya[1] and On behalf of the 'Turkish Online Haemodiafiltration Study'

[1]Division of Nephrology, Ege University School of Medicine, Izmir, Turkey, [2]Fresenius Medical Care Dialysis Clinics, Turkey, [3]Division of Nephrology, Akdeniz University School of Medicine, Antalya, Turkey and [4]Division of Nephrology, Dicle University School of Medicine, Diyarbakir, Turkey

Correspondence and offprint requests to: Ercan Ok; E-mail: ercan.ok@ege.edu.tr



www.kidney-international.org

Kidney Int 2017

clinical trial

Treatment tolerance and patient-reported outcomes favor online hemodiafiltration compared to high-flux hemodialysis in the elderly

see commentary on page 1279

Marion Morena[1,2,3], Audrey Jaussent[4], Lotfi Chalabi[5], Hélène Leray-Moragues[6], Leila Chenine[6], Alain Debure[7], Damien Thibaudin[8], Lynda Azzouz[9], Laure Patrier[10], Francois Maurice[11], Philippe Nicoud[12], Claude Durand[13], Bruno Seigneuric[14], Anne-Marie Dupuy[1], Marie-Christine Picot[6], Jean-Paul Cristol[1,2,3] and Bernard Canaud[2,15]; for the FRENCHIE Study Investigators[16]

[1]*Laboratoire de Biochimie, CHU de Montpellier, Montpellier, France;* [2]*Institut de Recherche et de Formation en Dialyse, Montpellier, France;* [3]*PhyMedExp, INSERM U1046, CNRS UMR9214, Université de Montpellier, Montpellier, France;* [4]*Département de l'Information Médicale, CHU de Montpellier, Montpellier, France;* [5]*Association pour l'Installation à Domicile des Epurations Rénales (AIDER), Montpellier, France;* [6]*Service de Néphrologie, CHU de Montpellier, Montpellier, France;* [7]*ATS, Saint-Denis, France;* [8]*Service de Néphrologie, CHU de Saint Etienne, Saint-Etienne, France;* [9]*Association Régionale pour le Traitement de l'Insuffisance Rénale Chronique, Saint-Priest-en-Jarez, France;* [10]*AIDER, Nimes, France;* [11]*Centre Hémodialyse du Lez, Castelnau le Lez, France;* [12]*Centre de Néphrologie du Mont Blanc, Sallanches, France;* [13]*Polyclinique Saint Martin, Pessac, France;* [14]*Service de Néphrologie, CHU de Toulouse, Toulouse, France; and* [15]*Université de Montpellier, Néphrologie, Montpellier, France*

ckj
OXFORD
CKJ REVIEW

Clinical Kidney Journal, 2015, vol. 8, no. 4, 368–373

doi: 10.1093/ckj/sfv040
Advance Access Publication Date: 10 June 2015
CKJ Review

High convection volume in online post-dilution haemodiafiltration: relevance, safety and costs

Ira M. Mostovaya[1], Muriel P.C. Grooteman[2,3], Carlo Basile[4], Andrew Davenport[5],

Table 2. Summary of intervention and comparator arms in recent meta-analyses that compared convective therapies with diffusive therapies

Meta-analysis	Intervention arm	Comparator arm
Susantitaphong *et al.* [15]	- Haemodiafiltration - Haemofiltration - High-flux haemodialysis	- Low-flux haemodialysis
Wang *et al.* [16]	- Post-dilution haemodiafiltration - Pre-dilution haemodiafiltration - Paired online haemodiafiltration - Haemofiltration - Acetate-free biofiltration	- Low-flux haemodialysis - High-flux haemodialysis
Nistor *et al.* [17]	- Online haemodiafiltration - Offline haemodiafiltration - Haemofiltration - Acetate-free biofiltration	- Low-flux haemodialysis - High-flux haemodialysis
Mostovaya *et al.* [2]	- Online post-dilution haemodiafiltration - Offline post-dilution haemodiafiltration - Pre-dilution haemodiafiltration	- Low-flux haemodialysis - High-flux haemodialysis

Online post-dilution HDF → *Effetto positivo su mortalità*

Mortality rates and convection volumes

Table 1. Mortality rates in randomized controlled trials and observational studies stratified and arranged by convection volumes, on-treatment analyses

Reference	CV# (L/treatment)[a]	SV## (L/treatment)[b]	IDWL (L/treatment)	HR	95% CI of HR
ESHOL[c]	<23.1			0.90	0.61–1.31
2013 [9]	23.1–25.4			0.60	0.39–0.90
	>25.4			0.55	0.34–0.84
Turkish HDF study[d]	18.8	16.2	2.6	1.10	0.68–1.76
2013 [11]	20.3	18.1	2.2	0.54	0.31–0.93
CONTRAST[c]	<18.18			0.80	0.52–1.24
2012 [10]	18.18–21.95			0.84	0.54–1.29
	>21.95			0.61	0.38–0.98
RISCAVID[e]		14		0.69	
2008 [6]		23		0.46	
DOPPS		5.0–14.9		0.93	
2006 [5]		15.0–24.9		0.65	
EUCLID 2015 [7]	22.2	19.9		0.62	0.42–0.93
Imamovic *et al.*[d]		<20.4		0.84	0.46–1.53
2014		>20.4		0.29	0.13–0.68

[a]Sum of the intradialytic weight loss and the amount of substitution fluid.
[b]The amount of fluid infused into the bloodstream to compensate for water and solute movement from the blood to the dialysate.
[c]In ESHOL and CONTRAST, survival risks were reported by tertiles of convection volume (CV).
[d]In the Turkish HDF study and Imamovic *et al.*, survival risks were reported for patients above and below the median SV (17.6 L).
[e]In RISCAVID, 'Relative Risks' (and not HRs) are reported for offline HDF treatment (mean SV 14 L) and online HDF (mean SV 23 L).
CI, confidence interval; CONTRAST, CONvective TRAnsport STudy; CV, convection volume (SV + net ultrafiltration); DOPPS, Dialysis Outcomes and Practice Patterns Study; ESHOL, Estudio de Supervivencia de Haemodiafiltration On-Line; HDF, Haemodiafiltration; HR, hazard ratio; IDWL, interdialytic weight loss; RISCAVID, RISchio CArdiovascolare nei pazienti afferenti all' Area Vasta In Dialisi; EUCLID, European CLInical Database; SV, substitution volume.

Cochrane Library

Cochrane Database of Systematic Reviews

HDF appeared **to reduce cardiovascular, but not all-cause,mortality** and had uncertain effects on non-fatal cardiovascular events and hospitalisation compared to HD.

The quality of evidence was considered low due to methodological limitations and **poor reporting of the primary studies**

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of partici-pants (stud-ies)	Quality of the evidence (GRADE)	Comments
	Assumed risk Diffusion	Corresponding risk Convection				
All-cause mortality	200 per 1000	Not significant	RR 0.87 (0.72 to 1.05)	11 (3396)	⊕⊕⊝⊝ **low**	Convective therapy has little or no effect on all-cause mortality
Cardiovascular mortality	100 per 1000	75 per 1000	RR 0.75 (0.81 to 0.92)	6 (2889)	⊕⊕⊝⊝ **low**	Convective therapy may reduce cardiovascular mor-tality
Nonfatal cardiovas-cular events	130 per 1000	Not significant	RR 1.23 (0.93-1.63)	2 (1688)	⊕⊝⊝⊝ **very low**	Convective therapy has uncertain effects on non-fatal cardiovascular events
Health-related quality of life	Not estimable	Not estimable	Not estimable	8 (988)	⊕⊕⊝⊝ **very low**	Convective therapy has uncertain effects on health-re-lated quality of life

*The **assumed risk** (e.g. the median control group risk across studies) is derived from data within dialysis registries for all-cause mortality and cardiovascular mortality and the reported event rate in the available study for nonfatal cardiovascular events (CONTRAST (Dutch) Study 2005). The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** Confidence interval; **RR:** Risk Ratio

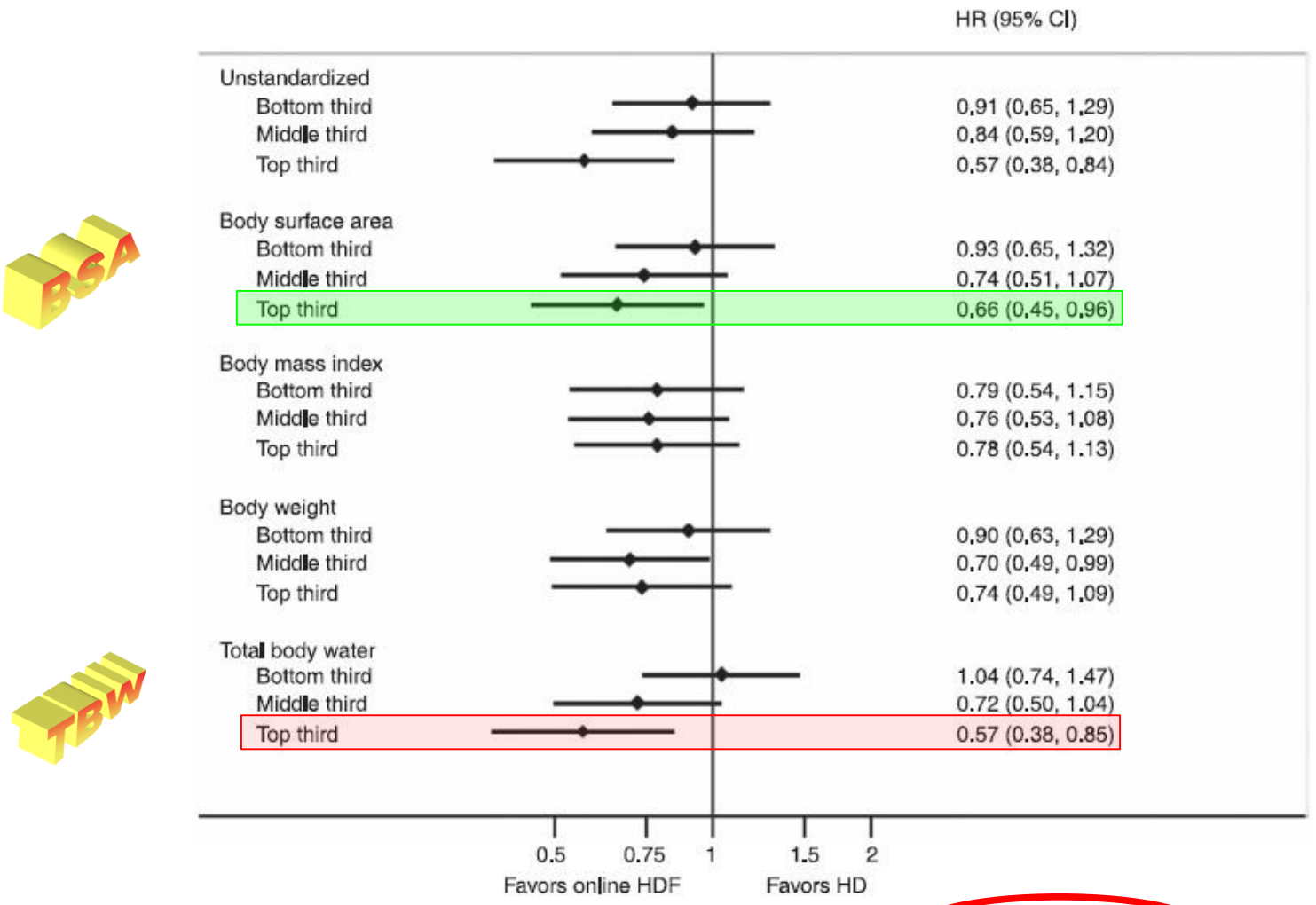
GRADE (Grading of Recommendations Assessment, Development, and Evaluation) Working Group grades of evidence (Guyatt 2011).
Low quality: Indicates that our confidence in the effect estimate is limited: The true effect may be substantially difference from the estimated effect.
Very low quality: Indicated that we have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimated effect.

http://www.kidney-international.org clinical investigation

Higher convection volume exchange with online hemodiafiltration is associated with survival advantage for dialysis patients: the effect of adjustment for body size

Hanno bisogno dello stesso volume convettivo?

Higher convection volume exchange with online hemodiafiltration is associated with survival advantage for dialysis patients: the effect of adjustment for body size



BSA

TBW

Figure 2 | Hazard ratios (HRs; boxes) and 95% confidence intervals (CI; bars) for cardiovascular mortality in patients receiving online hemodiafiltration versus hemodialysis by convection volume, using different methods to standardize convection volume.

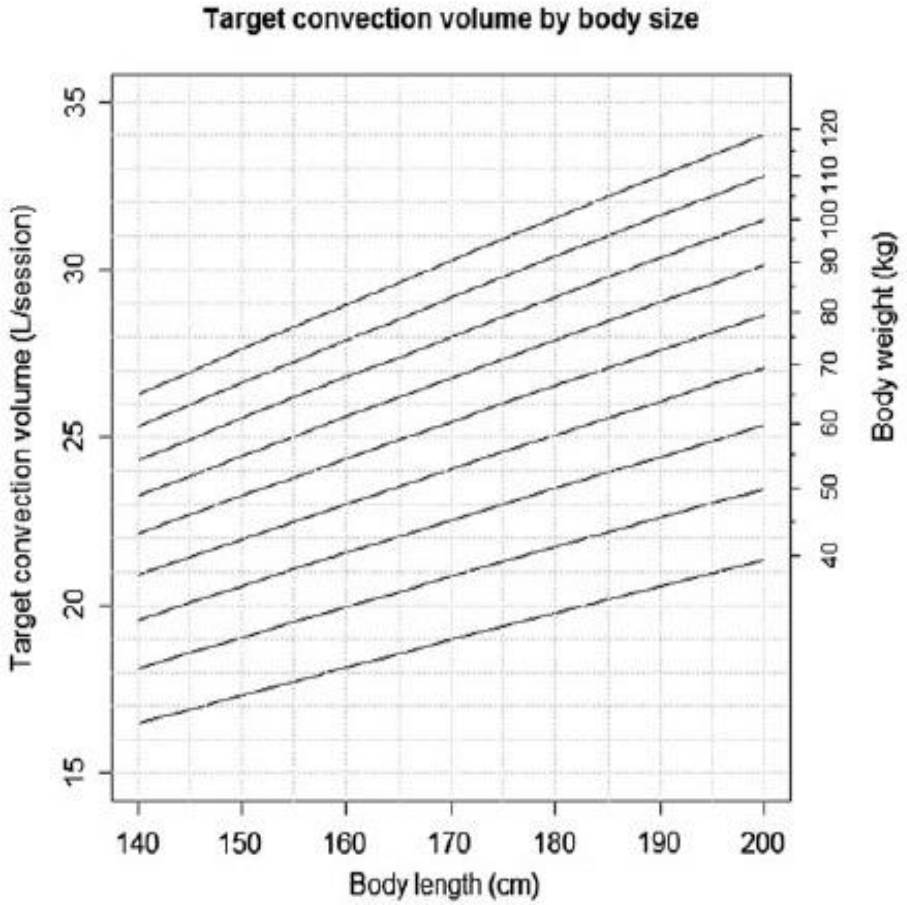
NDT Advance Access published October 22, 2015

Nephrol Dial Transplant (2015) 0: 1–7
doi: 10.1093/ndt/gfv349

Original Article

Haemodiafiltration and mortality in end-stage kidney disease patients: a pooled individual participant data analysis from four randomized controlled trials

Sanne A.E. Peters[1,2], Michiel L. Bots[2], Bernard Canaud[3,4], Andrew Davenport[5], Muriel P.C. Grooteman[6],



Convection volume/session needed for an individual patient to have a BSA-adjusted convection volume of at least 23 L or above, based on measurements of height and weight of the patient.

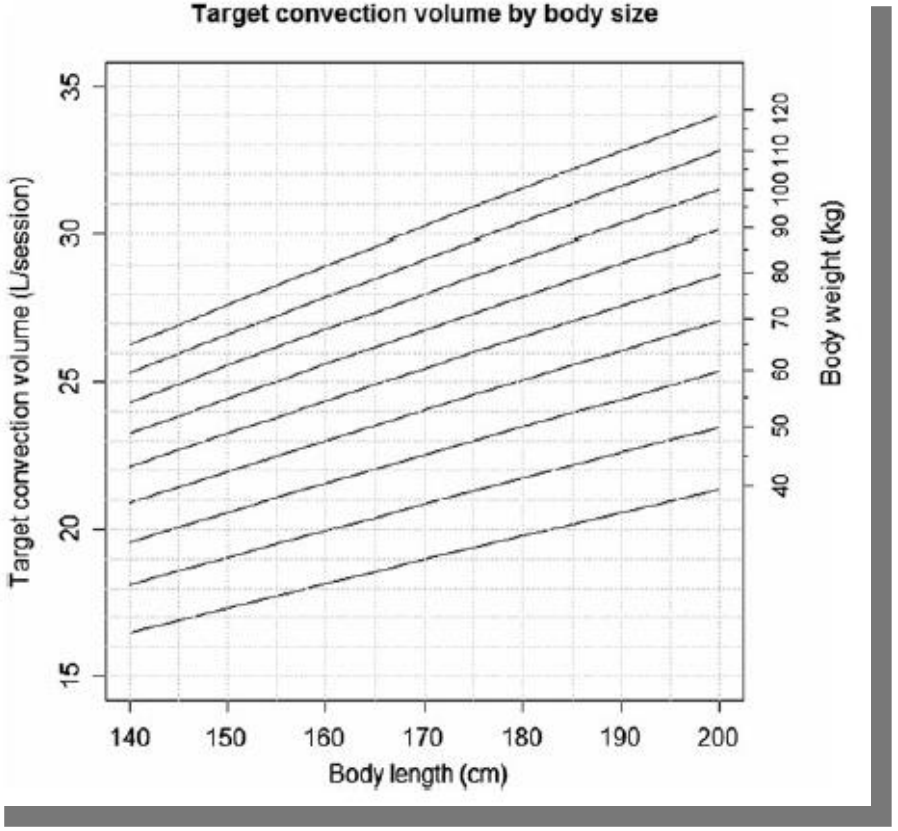
BSA was calculated using Formula Gehan and George as recommended by the European Best Practice Guidelines **[BSA (m2) = 0.0235 × baseline height (cm) 0.42246 × baseline weight (kg) 0.51456]**

Standardization of delivered convection volume was done by dividing by patient BSA **[1.73 × (patient convection volume/patient BSA)]**

HDF: 2013-2016

PETERS SA et al, 2016

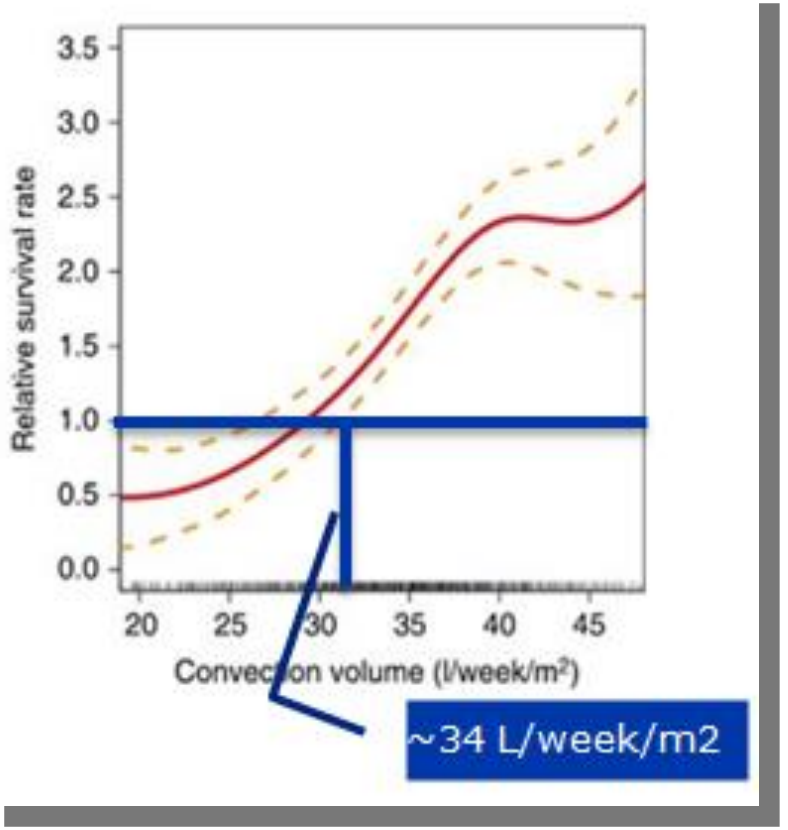
23 l / seduta / 1,73m²

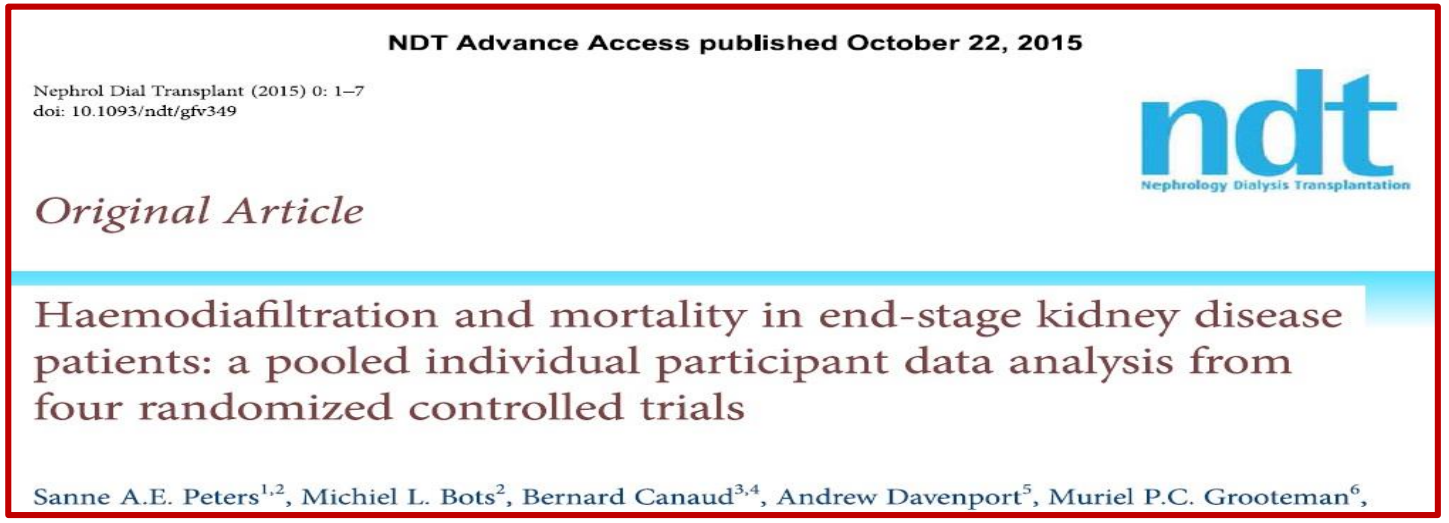


CANAUD B et al, 2015

>34 l / settimana / m²

>11 l / seduta / m²





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Original Article

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Sanne A.E. Peters[1,2], Michiel L. Bots[2], Bernard Canaud[3,4], Andrew Davenport[5], Muriel P.C. Grooteman[6],

The present combined analysis confirms this finding and suggests a substantial survival benefit when a convection volume of at least 23 L/session (BSA standardized) is delivered. Because almost all patients were treated in a thrice-weekly schedule, this dose equals at least ***69 L/week.***

Blood Purif 2018;46:7–11
DOI: 10.1159/000487918

Blood Purification

Is There Not Sufficient Evidence to Show That Haemodiafiltration Is Superior to Conventional Haemodialysis in Treating End-Stage Kidney Disease Patients?

Application of EBM related to end-stage kidney disease (ESKD) patients and renal replacement therapies is fraught with a number of difficulties

Blood Purif 2018;46:7–11
DOI: 10.1159/000487918

Blood Purification

Is There Not Sufficient Evidence to Show That Haemodiafiltration Is Superior to Conventional Haemodialysis in Treating End-Stage Kidney Disease Patients?

1° Randomized controlled studies are scarce, weak, or even inexistent

2° Most seminal interventional RCTs in dialysis have failed to reach their primary objective (e.g., the HEMO study , MPO study, Nocturnal FHN, IDEAL, 4D).

3° ESKD and uremia are highly complex pathologies that combine several metabolic disorders interacting with one another

4° Dialysis patients are mostly elderly (~2/3 are over 65 years) often having multiple comorbid conditions (60% with past history of severe cardiovascular event)

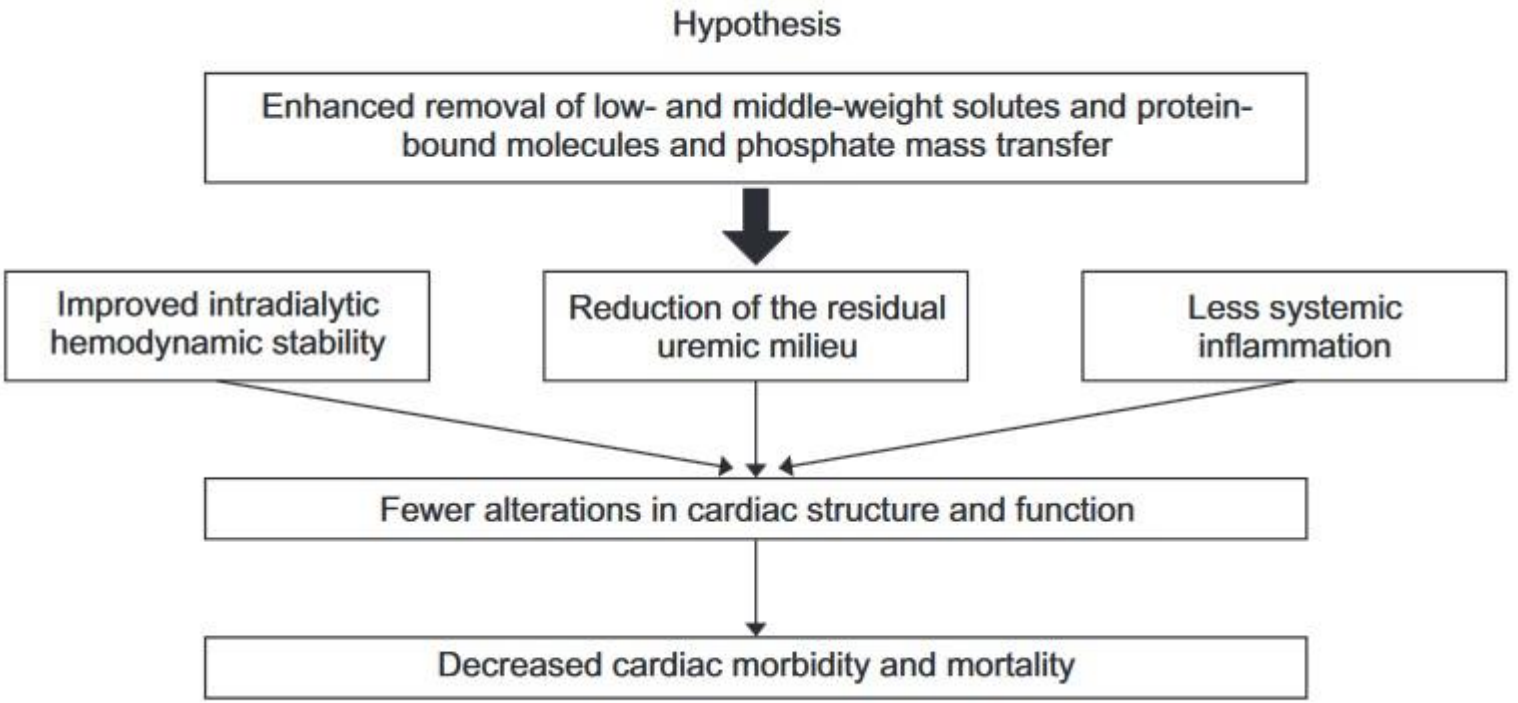
5° Practice patterns in the RRT field are highly diverse, as shown by the Dialysis Outcomes and Practice Patterns Study (DOPPS)

Review Article

Kidney Res Clin Pract 2019;38(2):159-168
pISSN: 2211-9132 • eISSN: 2211-9140
https://doi.org/10.23876/j.krcp.18.0160

KIDNEY RESEARCH AND CLINICAL PRACTICE

Online hemodiafiltration and mortality risk in end-stage renal disease patients: A critical appraisal of current evidence



Review Article

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https://doi.org/10.23876/j.krcp.18.0160

KIDNEY RESEARCH AND CLINICAL PRACTICE

Online hemodiafiltration and mortality risk in end-stage renal disease patients: A critical appraisal of current evidence

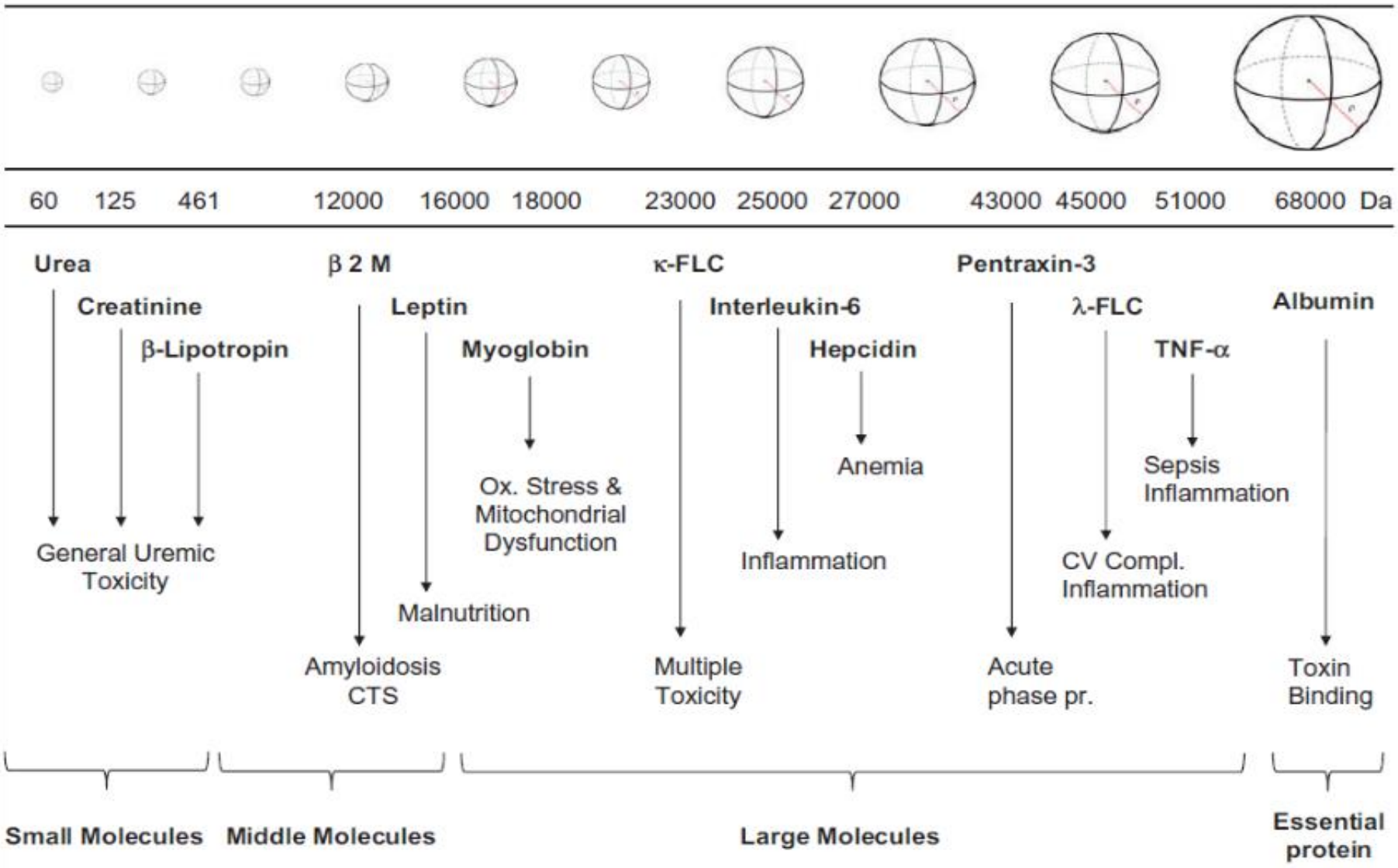
Table 1. Disadvantages of post-dilutional hemodiafiltration (HDF)

Theoretical risks
1. Transmission of infections or induction of inflammatory reactions related to the sterility of large amounts of substitution fluids directly infused into the patient
2. Loss of serum albumin, amino acids, or other hydrosoluble nutrients
3. Endothelial cell and blood cell activation during treatment

The Rise of Expanded Hemodialysis

Claudio Ronco[a, b]

Blood Purification

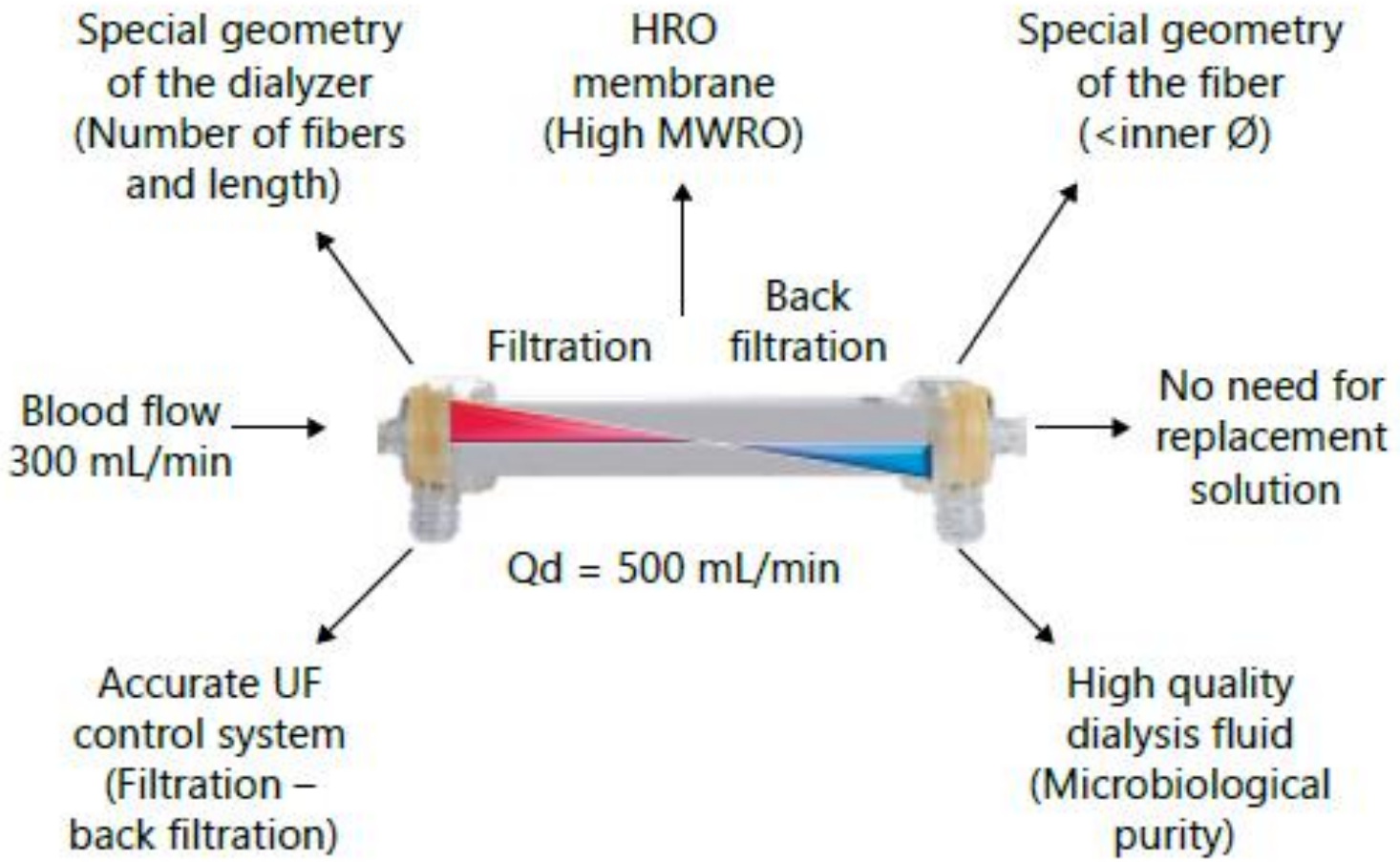


The Rise of Expanded Hemodialysis

Claudio Ronco[a, b]

Blood Purification

Expanded hemodialysis (HDx) and related operational parameters.



Nephrol Dial Transplant (2019) 34: 901–907
doi: 10.1093/ndt/gfy236
Advance Access publication 8 August 2018

ndt
Nephrology Dialysis Transplantation

Hypoalbuminemia: a price worth paying for improved dialytic removal of middle-molecular-weight uremic toxins?

Richard A. Ward[1], Werner Beck[2], Angelito A. Bernardo[3], Filipa C. Alves[4,5], Peter Stenvinkel[5] and Bengt Lindholm[5]

Category	Ultrafiltration coefficient[a] (mL/h/mmHg/m^2)	β_2-microglobulin clearance[b] (mL/min)	Albumin loss[c] (g)	Sieving coefficient[a]		Reference
				β_2-microglobulin	Albumin	
Low flux	<12	<10	0	–	0	[16]
High flux	14–40	20–40	<0.5	0.7–0.8	<0.01	[6]
MCO	40–60	>80	2–4	0.99	<0.01	[17, 18]
Protein leaking	>40	>80	2–6	0.9–1.0	0.01–0.03	[19]
HCO	40–60	–	9–23	1.0	<0.2	[20, 21]

Classificazione delle membrane per emodialisi

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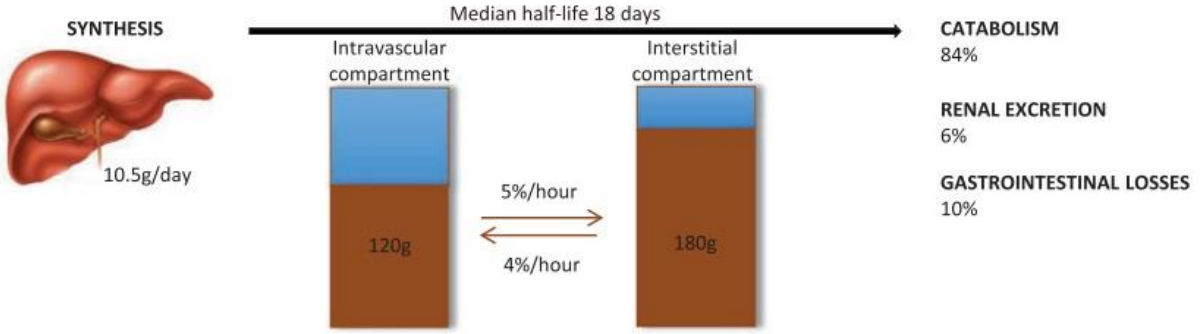
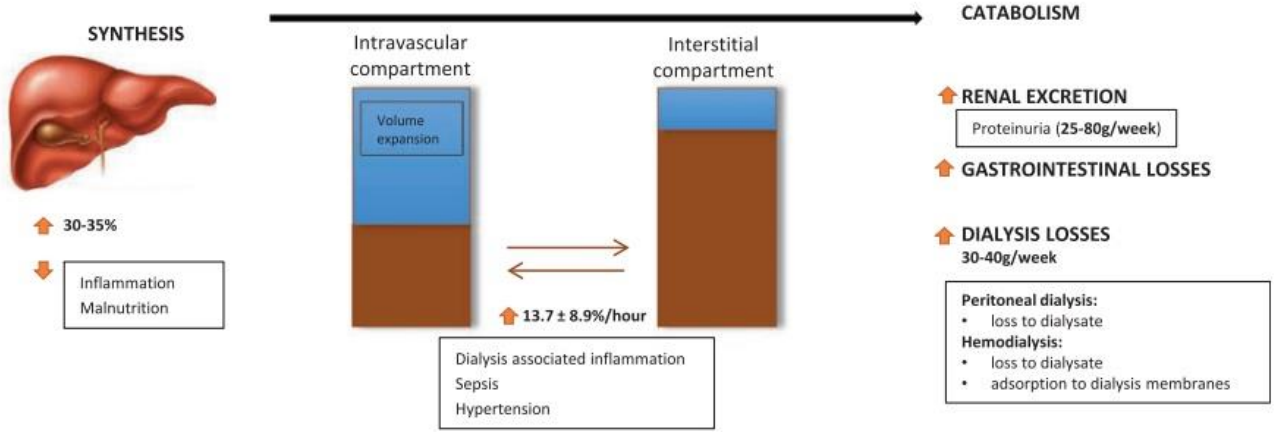
Albumin homeostasis



Albumin homeostasis in ESKD



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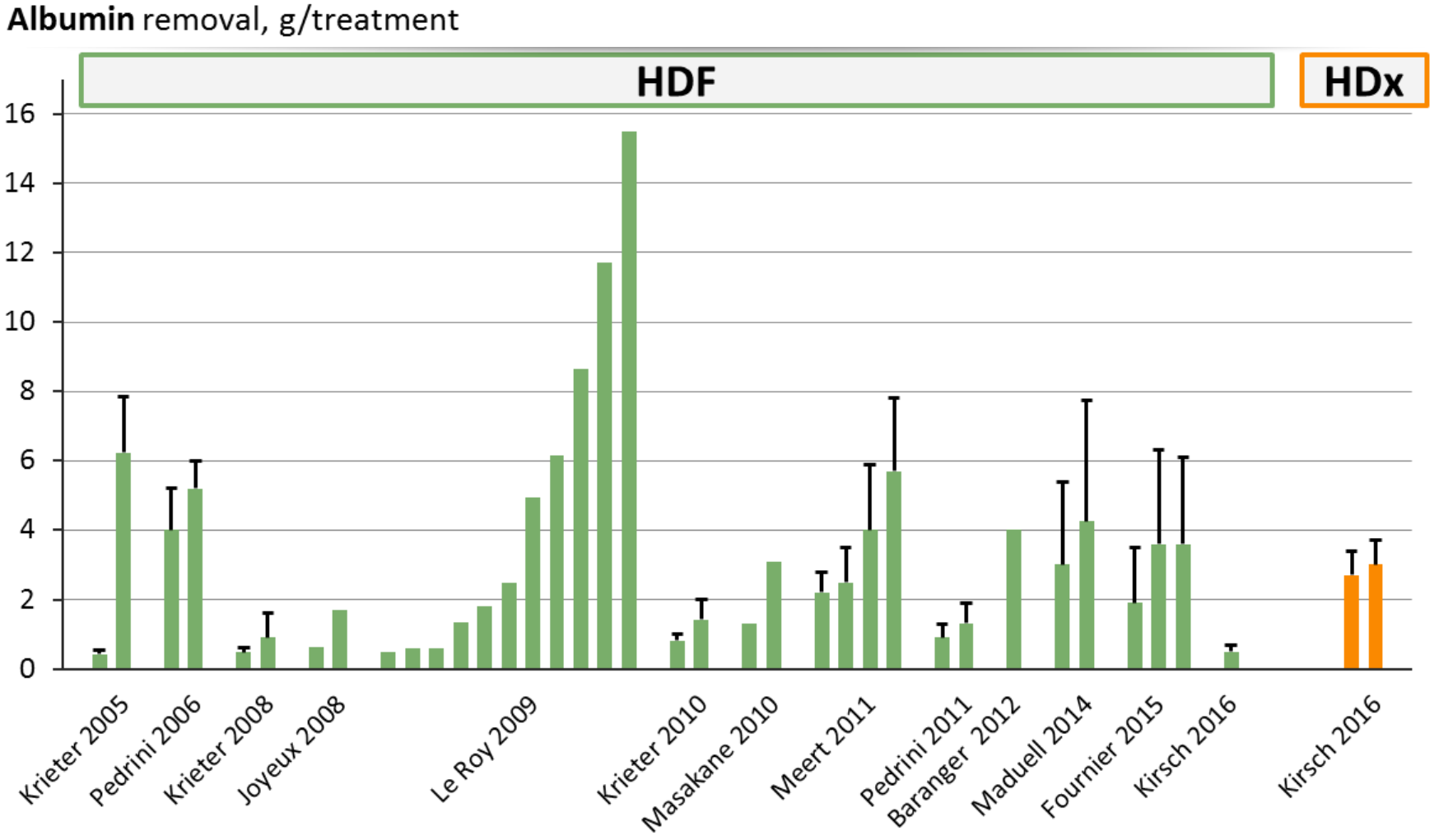
Hypoalbuminemia: a price worth paying for improved dialytic removal of middle-molecular-weight uremic toxins?

Richard A. Ward[1], Werner Beck[2], Angelito A. Bernardo[3], Filipa C. Alves[4,5], Peter Stenvinkel[5] and Bengt Lindholm[5]

Available data suggest a need for caution when contemplating routine use of dialyzers containing membranes that produce a loss of $\geq$20 g/week of albumin, whereas the use of dialyzers resulting in a weekly loss of $\leq$12 g appears to pose little risk to patients.

Rimozione di Albumina in HDF e HDx

Comparazione della rimozione di albumina dei filtri attualmente in commercio in HDF vs. HDx dalla letteratura



Review Article

Kidney Res Clin Pract 2019;38(2):159-168
pISSN: 2211-9132 • eISSN: 2211-9140
https://doi.org/10.23876/j.krcp.18.0160

KIDNEY RESEARCH AND CLINICAL PRACTICE

Online hemodiafiltration and mortality risk in end-stage renal disease patients: A critical appraisal of current evidence

Table 1. Disadvantages of post-dilutional hemodiafiltration (HDF)

Theoretical risks
1. Transmission of infections or induction of inflammatory reactions related to the sterility of large amounts of substitution fluids directly infused into the patient
2. Loss of serum albumin, amino acids, or other hydrosoluble nutrients
3. Endothelial cell and blood cell activation during treatment
Clinical practice
1. There is no published literature showing any undesirable effect of post-dilution HDF or superiority of standard high-flux hemodialysis over post-dilution online HDF.

Clinical Kidney Journal

Personalizing treatment in end-stage kidney disease: deciding between haemodiafiltration and haemodialysis based on individualized treatment effect prediction

Previous studies suggest that haemodiafiltration (HDF) reduces mortality compared with haemodialysis (HD) in patients with end-stage kidney disease (ESKD), but controversy surrounding its benefits remain and it is unclear to what extent individual patients benefit from HDF.

Methods

4 randomized controlled trials (N = 2793 patients)

HDF vs. HD

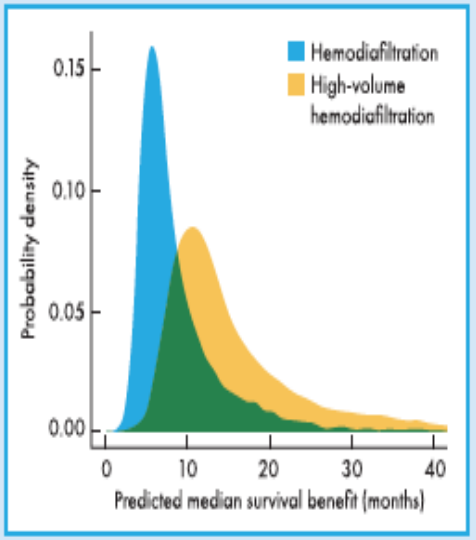
Royston-Parmar model for prediction of absolute treatment effect

Results

Median predicted survival benefit was **44 days for every year of treatment with HDF**

Patients who benefited most from HDF were:

- younger
- less likely to have diabetes or CV disease
- higher serum creatinine and albumin levels



An online calculator for the model is available at: https://hdfpredictiontool.shinyapps.io/hdf_prediction_tool/

Conclusion: The median survival benefit of HDF compared to HD can be predicted and compared for individual patients using a combination of readily available patient and disease characteristics, which could guide shared decision-making.

Robin W.M. van Kruijsdijk et al.
Clinical Kidney Journal (2022)
r.w.m.vernooij-2@umcutrecht.nl
@CKJsocial

Keywords: haemodiafiltration, haemodialysis, treatment effect heterogeneity, treatment effect prediction

Online hemodiafiltration in post-dilution mode:

Present knowledge:

- Suggestion of a reduction in all cause mortality, in particular CV mortality
- Especially when convection volume > 23 L/session (i.e. 69 L/week)
- In previous studies convection volume > 23 L/4h was only delivered in minority of patients
- No clear side effects, no clear safety issues
- Mechanism(s): not fully clear

CONVINCE will deliver definite proof of superiority yes/no.

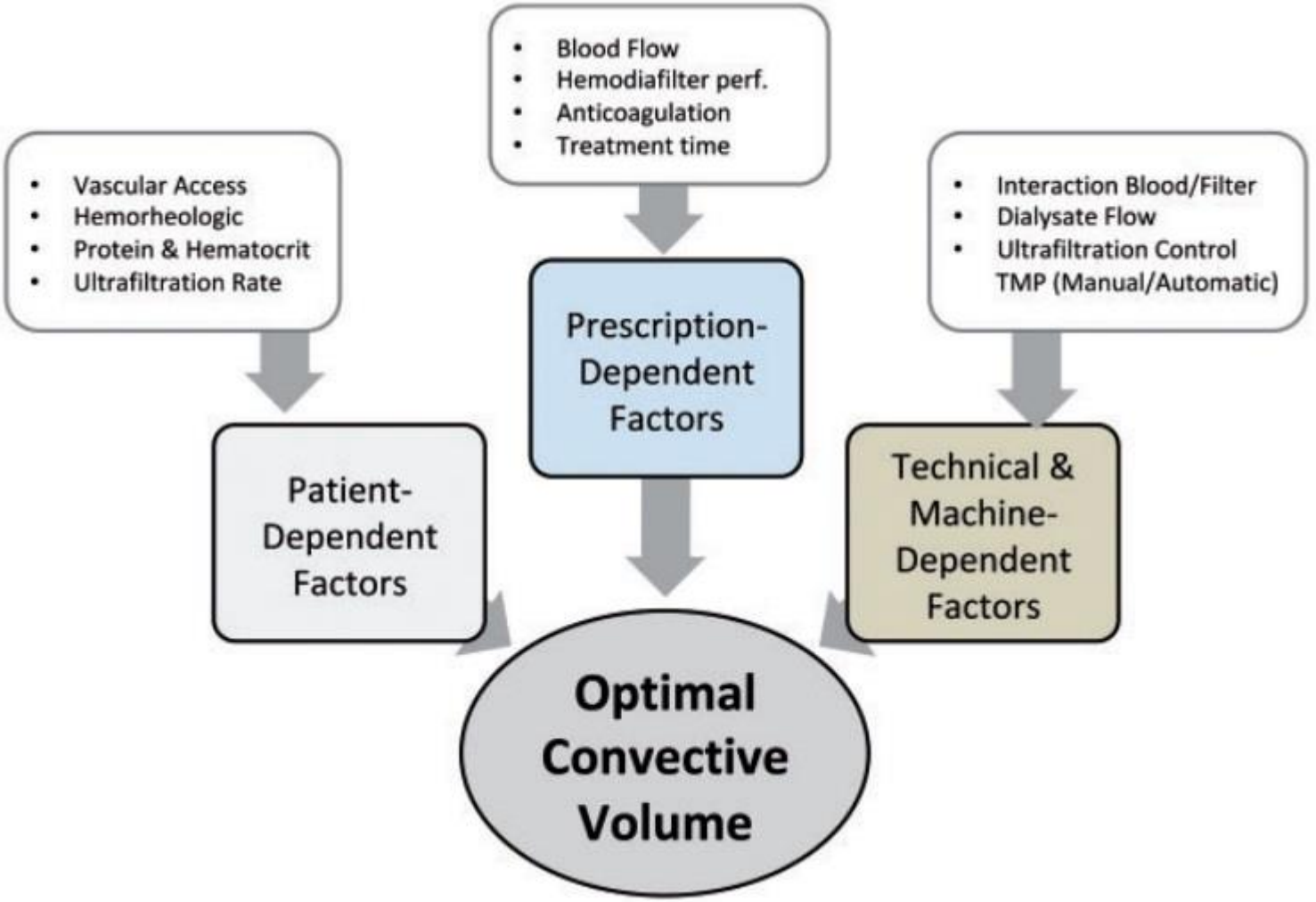
UMC Utrecht
Center for Circulatory Health

Nephrol Dial Transplant (2019) 1–10
doi: 10.1093/ndt/gfz005

ndt
Nephrology Dialysis Transplantation

Global prevalent use, trends and practices in haemodiafiltration

Bernard Canaud[1,2], Katrin Köhler[1], Jan-Michael Sichart[3] and Stefan Möller[3]

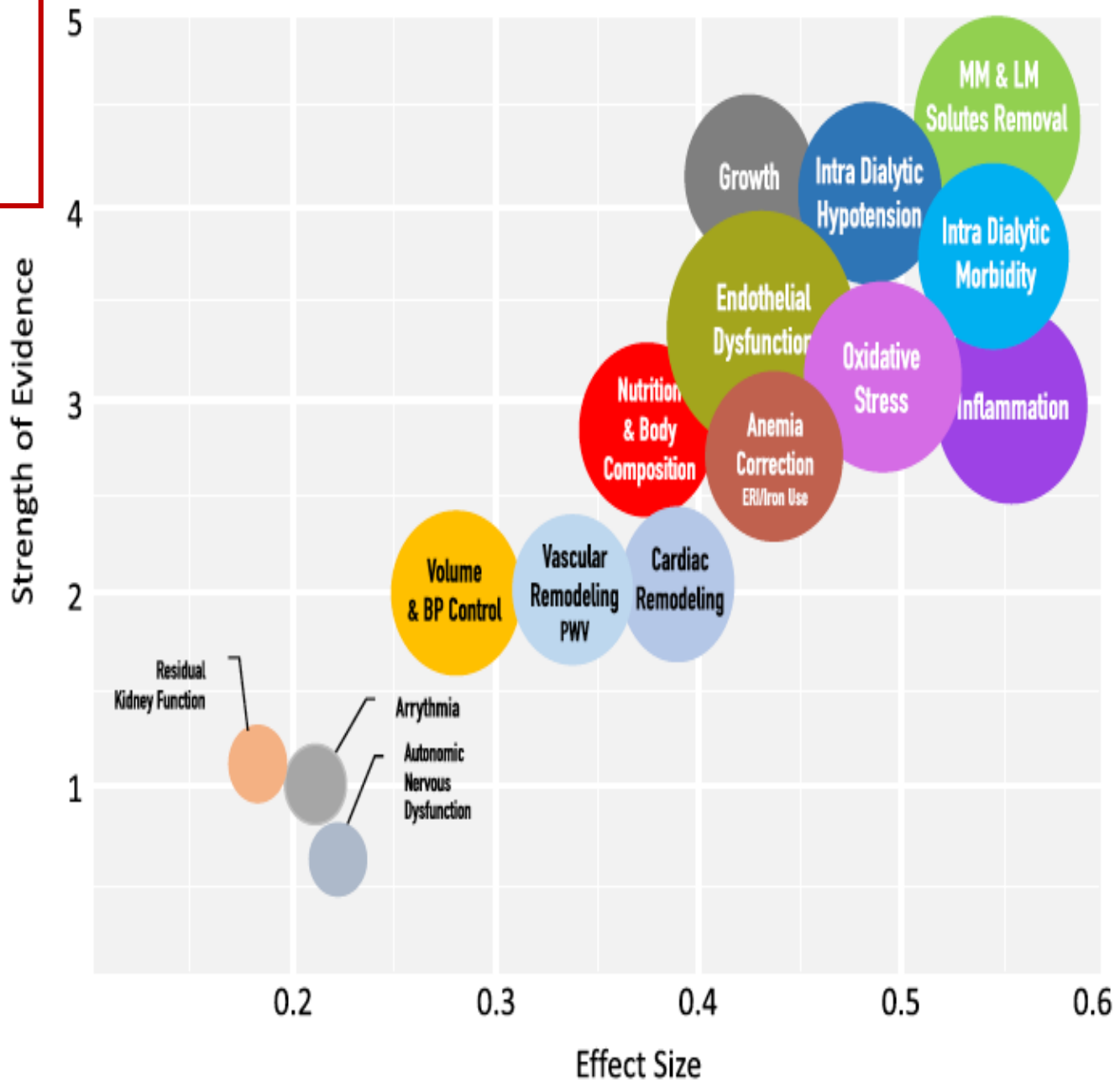


Received: 15 April 2021 | Revised: 26 July 2021 | Accepted: 27 July 2021
DOI: 10.1111/sdi.13039

Seminars in Dialysis WILEY

REVIEW ARTICLE

Why and how high volume hemodiafiltration may reduce cardiovascular mortality in stage 5 chronic kidney disease dialysis patients? A comprehensive literature review on mechanisms involved



Nephrol Dial Transplant (2022) 37: 1006–1013
https://doi.org/10.1093/ndt/gfac019
Advance Access publication date 31 January 2022

CONVINCE in the context of existing evidence on haemodiafiltration

Table 1. Current knowledge on haemodiafiltration (HDF) versus haemodialysis (HD) stratified by study design

Study design	Potential limitations of the study design	Results on HDF versus HD
Individual-patient data meta-analysis	• Not designed to study the effects of dosage of convection volumes • Heterogeneity across studies in HDF techniques	• Online HDF reduced the risk of all-cause mortality by 14% [95% confidence interval (CI): 1%; 25%] and cardiovascular mortality by 23% (95% CI: 3%; 39%). The largest survival benefit was for patients receiving the highest delivered convection volume, with a multivariable-adjusted hazard ratio (HR) of 0.78 (95% CI 0.62–0.98) for all-cause mortality and 0.69 (95% CI 0.47–1.00) for cardiovascular disease mortality [13].
Systematic reviews of randomized controlled trials	• High risk of bias of included studies (e.g. on allocation concealment, blinding, incomplete reporting) • Not designed to study the effects of convection volumes • Heterogeneity across studies in HDF techniques	• Convective dialysis (i.e. HF, HDF and acetate-free biofiltration) had no significant effect on all-cause mortality [relative risk (RR) 0.87, 95% CI 0.72–1.05], but significantly reduced cardiovascular mortality (RR 0.75, 95% CI 0.61–0.92). Sensitivity analyses limited to studies comparing HDF with HD showed very similar results. [12]. • In a meta-analysis of 6 RCTs, HDF treatment was related to a decreased risk of mortality (RR 0.84, 95% CI 0.73–0.96) and cardiovascular death (RR 0.73, 95% CI 0.57–0.92) compared with HD [14].
Observational studies	• Confounding by indication • Residual confounding • Evidence of association, not causation	• Adjusted mortality HR (95% CI) was 1.14 (1.00–1.29) for any HDF versus HD and 1.08 (0.92–1.28) for HDF >20 L replacement fluid volume versus HD [3]. • When compared with HD, HDF treatment was associated with reduced mortality in the multivariate survival analysis (HR 0.58, 95% CI 0.36–0.93) [8]. • A statistically significant survival advantage of HV-HDF (odds ratio 0.501, CI 0.366–0.684) [9]. • HRs for all-cause and cardiovascular mortality associated with HDF use were 0.84 (95% CI 0.77–0.91) and 0.73 (95% CI 0.61–0.88), respectively [10]. • Substitution volume between 21 and 25 L/session was associated with longer 5-year survival [11].

*The RCTs were not designed to study the effects of convection volumes, with **no randomized treatment targets and hence the possibility of confounding by indication cannot be excluded** …..*

Open access Protocol

BMJ Open

Benefits and harms of high-dose haemodiafiltration versus high-flux haemodialysis: the comparison of high-dose haemodiafiltration with high-flux haemodialysis (CONVINCE) trial protocol

Peter J Blankestijn,[1] Kathrin I Fischer,[2] Claudia Barth,[3] Krister Cromm ,[4] Bernard Canaud,[4,5] Andrew Davenport,[6] Diederick E Grobbee,[7,8] Jörgen Hegbrant,[9] Kit C Roes,[7] Matthias Rose,[2,10] Giovanni FM Strippoli,[11,12] Robin WM Vernooij ,[1,7] Mark Woodward,[13,14,15] G Ardine de Wit,[7,16] Michiel L Bots[7]

Strengths and limitations of this study

- This is the largest randomised trial to assess the efficacy and safety of high-dose haemodiafiltration versus continuation of conventional high-flux haemodialysis in patients with end-stage kidney disease (ESKD).
- Information will be collected about patient-reported outcomes, particularly health-related quality of life.
- A cost-effectiveness analysis for the two treatment modalities will be performed.
- Information about co-medications, given that patients with ESKD have often comorbidities, will be collected during follow-up.

Study objectives

Based on previous evidence, we hypothesise that high-dose HDF will significantly decrease mortality risk compared to conventional high-flux HD treatment in adults with ESKD. The objectives of our study are:

1. To evaluate the comparative efficacy of high-dose HDF and high-flux HD on all-cause and cause-specific death, fatal and non-fatal cardiovascular events, all-cause and cause-specific hospitalisations.
2. To evaluate the effect of high-dose HDF versus high-flux HD on patient-reported outcomes (PROs), particularly health-related quality of life.
3. To conduct a cost-effectiveness analysis for the two treatment modalities.

Open access Protocol

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….on the 2.5-year mortality rate, an estimated number of participants of **900 (HR 0.75) per group will need to be recruited**. Thus, the total sample size will be **1800 participants to be randomised**. We intend to recruit **400 from academic and hospital** based-dialysis centres and **1400 from private dialysis providers…**

Table 1 Inclusion and exclusion criteria for enrolment in CONVINCE

Inclusion criteria	A participant must meet ALL of the following criteria in order to participate: 1. Signed and dated written Informed Consent Form obtained from the participant or his/her guardian or in accordance with local regulations. 2. Aged ≥18 years. 3. Diagnosed with ESKD. 4. On HD treatment for ≥3 months. 5. Likely to achieve high-dose HDF (≥23 L, in postdilution mode), according to the protocol. 6. Willing to have a dialysis session with duration of ≥4 hours, three times a week. 7. Understands study procedures and is able to comply.
Exclusion criteria	A participant who meets any of the following criteria will be excluded from participation: 1. Severe participant non-compliance defined as severe non-adherence to the dialysis procedure and accompanying prescriptions, especially frequency and duration of dialysis treatment. 2. Life expectancy <3 months. 3. HDF treatment <90 days before screening. 4. Anticipated living donor kidney transplantation <6 months after screening. 5. Evidence of any other diseases or medical conditions that may interfere with the planned treatment, affect participant compliance or place the participant at high risk for treatment-related complications. 6. Participation in any other study will be discussed with and decided by the Executive Board. 7. Unavailable ≥3 months during the study conduct for study visits.

ESKD, end-stage kidney disease; HD, haemodialysis; HDF, haemodiafiltration.

Table 2 Achieving convection volume ≥23 L/treatment session

	Processed BV (L)‡	FF 20	21	22	23	24	25	26	27	28	29	30	31*
Treatment time 3.5 hours													
Qb† 300 mL/min	63.0	12.6	13.2	13.9	14.5	15.1	15.8	16.4	17.0	17.6	18.3	18.9	19.5
Qb 350 mL/min	73.5	14.7	15.4	16.2	16.9	17.6	18.4	19.1	19.8	20.6	21.3	22.1	22.8
Qb 400 mL/min	84.0	16.8	17.6	18.5	19.3	20.2	21.0	21.8	22.7	23.5	24.4	25.2	26.0
Treatment time 4.0 hours													
Qb 300 mL/min	72.0	14.4	15.1	15.8	16.6	17.3	18.0	18.7	19.4	20.2	20.9	21.6	22.3
Qb 350 mL/min	84.0	16.8	17.6	18.5	19.3	20.2	21.0	21.8	22.7	23.5	24.4	25.2	26.0
Qb 400 mL/min	96.0	19.2	20.2	21.1	22.1	23.0	24.0	25.0	25.9	26.9	27.8	28.8	29.8
Treatment time .4.5 hours													
Qb 300 mL/min	81.0	16.2	17.0	17.8	18.6	19.4	20.3	21.1	21.9	22.7	23.5	24.3	25.1
Qb 350 mL/min	94.5	18.9	19.8	20.8	21.7	22.7	23.6	24.6	25.5	26.5	27.4	28.4	29.3
Qb 400 mL/min	108.0	21.6	22.7	23.8	24.8	25.9	27.0	28.1	29.2	30.2	31.2	32.4	33.5

Assessment of patient-reported outcomes

Box 1 List of the patient reported outcomes (PROs questionnaires in CONVINCE)

Instruments included in the initial assessment tools are:
- Sociodemographic variables & treatment information.
- PROMIS Fatigue 6-item customised short form.
- Time to recovery module.
- Modified Kidney Disease Quality of Life (KDQOL) symptom checklist.
- Health transition items (2 items of the SF-36).
- PROMIS Physical Function 4-item short form (part of the PROMIS Profile-29).
- PROMIS Cognitive Abilities 4-item customised short form.
- PROMIS Pain Interference 4-item short form (part of the PROMIS Profile-29).
- PROMIS Pain Intensity one item (part of the PROMIS Profile-29).
- PROMIS Anxiety 4-item short form (part of the PROMIS Profile-29).
- PROMIS Depression 4-item short form (part of the PROMIS Profile-29).
- PROMIS Ability to participate in social roles and activities 4-item short form (part of the PROMIS Profile-29).
- PROMIS Sleep disturbance 4-item short form (part of the PROMIS Profile-29).

- Two items time to recovery module.
- PROMIS Depression 3item short form (part of the PROMIS Profile-29).
- PROMIS Ability to participate in social roles and activities 3-item short form (part of the PROMIS Profile-29).

Based on the technical infrastructure and the availability of PROMIS item banks in participating countries (availability of translations) computer-adaptive tests (CATs) might replace the respective PROMIS short forms.

- Perceived Stress Questionnaire 5-item short form.
- 5-item sub-set of the General Self-Efficacy Scale.[47]
- MOS Social Support Scale 4-item short form.

The Patient Health Assessment Quarterly (PHA-Quarterly) is a comprehensive assessment of the participants health status, which includes the core instruments of the screening instruments:
- PROMIS Fatigue 6-item customised short form.
- Time to recovery module.
- modified KDQOL symptom checklist.
- 2 Health transition items (SF-36)–modified.
- PROMIS Physical Function 5-item short form (part of the PROMIS Profile-29).
- PROMIS Cognitive Abilities 4-item customised short form.
- PROMIS Pain Interference 4-item short form (part of the PROMIS Profile-29).
- PROMIS Pain Intensity 1-item (part of the PROMIS Profile-29).
- PROMIS Anxiety 4-item short form (part of the PROMIS Profile-29).
- PROMIS Depression 4-item short form (part of the PROMIS Profile-29).
- PROMIS Ability to participate in social roles and activities 4item short form (part of the PROMIS Profile-29).
- PROMIS Sleep disturbance 4-item short form (part of the PROMIS Profile-29).

The Patient Health Assessment Monthly (PHA-Monthly) will monitor the health status monthly with a parsimonious assessment of key health domains, including fatigue, physical function, depression, social participation and items asking about the recovery time. Instruments included for the monthly assessment are:
- Modified transition question (SF-36).
- PROMIS Physical Function 3-item short form (part of the PROMIS Profile-29).
- PROMIS Fatigue 3-item short form (part of the PROMIS Profile-29).

-astenia
-dolore
-capacità cognitive
-ansia,depressione
-vita sociale
-disturbi del sonno...

Cost–utility analysis and budget-impact analysis

- valutazione economica che esprima : costi per qualità di anno di vita (Quality-Adjusted-Life-Year QALY)

Le fonti per la valutazione saranno:

- il paziente e i medici riporteranno utilizzo del sistema sanitario (costi sanitari oltre la dialisi)

- il paziente riporterà costi per lui/famiglia (cure non sostenute dal sistema sanitario, perdita di giornate di lavoro o reddito)


Recruitment & Site Status
Recruiting sites
Actual
Enrolled patients
Sites
0
200
400
600
800
1000
1200
1400
1600
0
10
20
30
40
50
60
70
15
118
150
176
206
246
307
425
517
593
625
653
670
674
753
918
1023
1075
1087
1131
1202
1313
1360
May-19
Jun-19
Jul-19
Aug-19
Sep-19
Oct-19
Nov-19
Dec-19
Jan-20
Feb-20
Mar-2020
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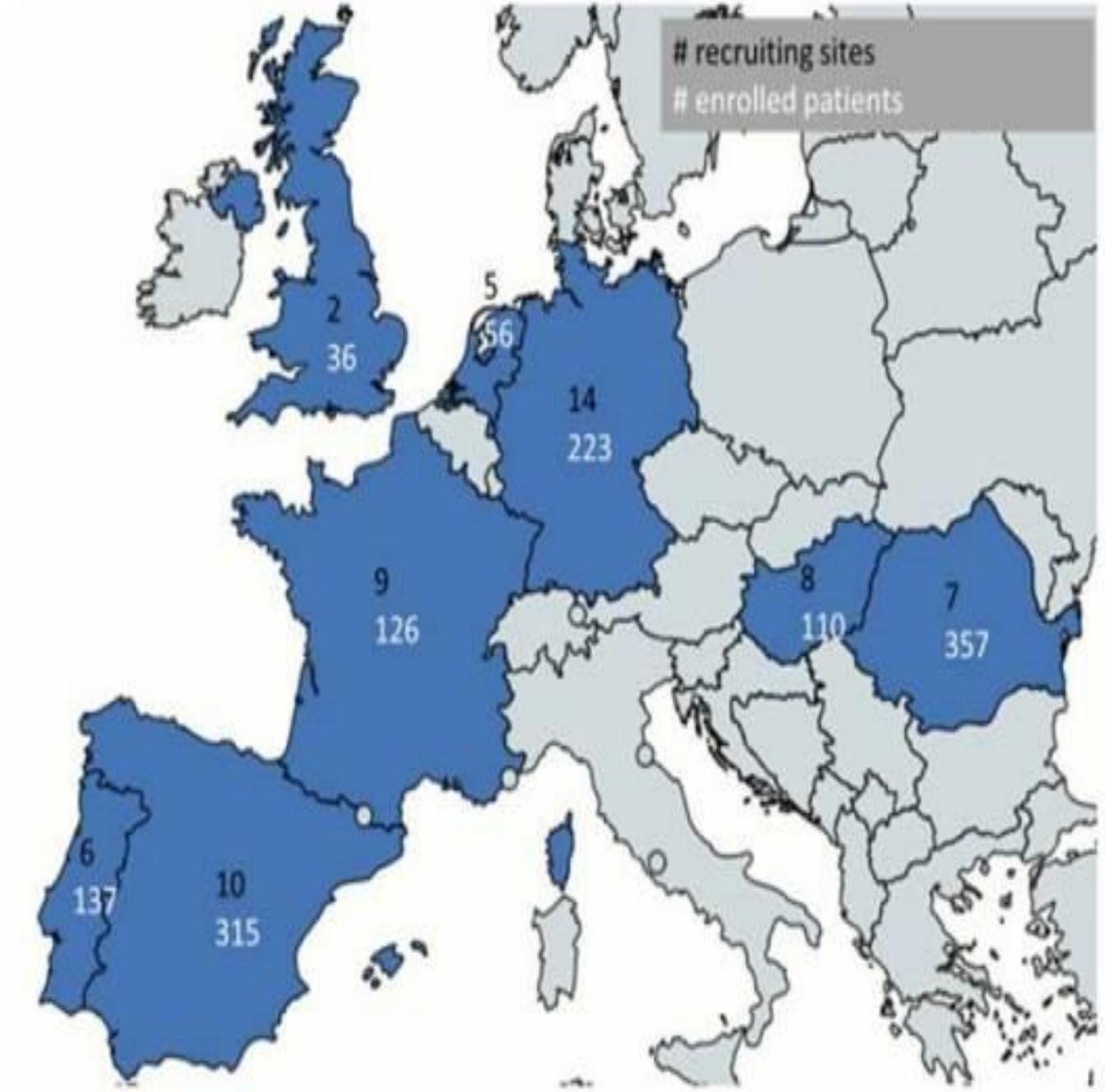
Oct-20
Nov-20
Dec-20
Jan-21
Feb-21
Mar-21


recruiting sites
enrolled patients
2
36
5
56
14
223
9
126
8
110
7
357
6
137
10
315

Clin Kidney J (2015) 8: 191–198
doi: 10.1093/ckj/sfv003
Advance Access publication 16 February 2015

ckj

Haemodiafiltration

CKJ Review

Optimization of the convection volume in online post-dilution haemodiafiltration: practical and technical issues

Isabelle Chapdelaine[1], Camiel L.M. de Roij van Zuijdewijn[1], Ira M. Mostovaya[2], Renée Lévesque[3], Andrew Davenport[4], Peter J. Blankestijn[2], Christoph Wanner[5], Menso J. Nubé[1,6] and Muriel P.C. Grooteman[1,6], on behalf of the EUDIAL Group

EUropean DIALysis (EUDIAL) Working Group by the European Renal Association-European Dialysis and Transplant Association (ERAEDTA)

PROF.ERNESTO BIGNAMI

1931

Type of vascular access

>21 L of convection volume was achieved in **>84%** of patients with **AV fistula**, and in only **33%** of patients with a **catheter**. Hence, it appears that an AV fistula or graft is preferable, but a catheter is not a contra indication for the performance of ol HDF.

Needle size

With the exception of initial cannulation, in most guidelines no specific gauge value is recommended and the sole statement made is that “needle size should match the blood flow rate“. Only in the Fistula First Initiative is a **15G-needle** recommended for a blood flow between 350 and 450 mL/min.

Single-needle

Given the current high convection volume goals, single-needle ol-HDF should **not be** encouraged.

Chapdelaine I, 2015

Access recirculation

When blood flow rate is increased,

recirculation may occur. As an increase in the size of the convection

volume by recirculation is inefficient and undesirable,

regular monitoring is advisable.

Effective versus set blood flow rates

It has been well established that the real blood flow rate is somewhat lower than the set value, and the higher blood pump speed, the wider the difference. This phenomenon is explained by partial collapse of the tubes at more negative pre-pump pressure. In addition, the type of access may also influence this discrepancy. Canaud et al. showed that a set blood flow of 350 mL/min resulted in a markedly lower real blood flow in a CVC than in an AVF (316 **±** 4 versus 342 **±** 4 mL/min). Obviously, **this phenomenon may be even more prominent in HDF because of a more negative pre-pump pressure than in conventional HD**.

Treatment time

Is one of the major determinants of convection volume. A simple calculation shows that an increase in treatment time with **1 h**, at a given blood flow rate of 400 mL/min and a FF of 25%, augments convection volume with **6 L**. Thus, with respect to high-volume ol-HDF, a long treatment time can compensate for a low blood flow rate. Moreover, a prolonged treatment time per se has been shown to improve haemodynamic instability, which in turn may contribute to a high convection volume.

Anticoagulation

Because a high FF induces considerable haemoconcentration and clotting within the dialyser, adequate anticoagulation with either unfractionated heparin or low molecular weight heparin (LMWH) is mandatory. In THDFS, the **unfractionated heparin dose was ~10% higher in the HDF group** when compared with HD patients

Dialyser

In order to avoid TMP alarms, it appears wise to avoid dialysers with a surface area **<1.7 m2** or dialysers with a high blood flow resistance.

DOBBIAMO PERSONALIZZARE IL TRATTAMENTO DIALITICO!!!


thank you
danke
謝謝
рахмат
ngiyabonga
teşekkür ederim
Баярлалаа
спасибо
faafetai lava
mersi
kia ora
barka
welalin
tack
spas
vinaka
спасибі
blagodaram
dank je
misaotra
matondo
paldies
grazzi
mahalo
gracias
tapadh leat
хвала
asante
manana
obrigada
tenki
murakoze
kiitos
dankie
nanni
nandri
dhanyavad
mauruuru
hvala
köszönöm
gràcie
bayarlalaa
bedankt
enkosi
dziękuję
dankon
akun
ačiū
djiere dieuf
tau
mochchakkeram
дякую
mamnun
chokrane
chnorakaloutioun
gratias ago
gràcies
sulpáy
taiku
go raibh maith agat
sobodi
dėkuji
obrigado
mèsi
didi madloba
sagolun
sukriya
kop khun krap
ありがとう
najis tuke
kam sah hamnida
rahmat
terima kasih
감사합니다
তোমাকে ধন্যবাদ
tanemirt
rahmet
grazie
xièxie
ευχαριστώ
diolch
dhanyavadagalu
arigatô
takk
dakujem
trugarez
shukriya
mercê
мерси
merci