Riccione, 16 aprile 2024

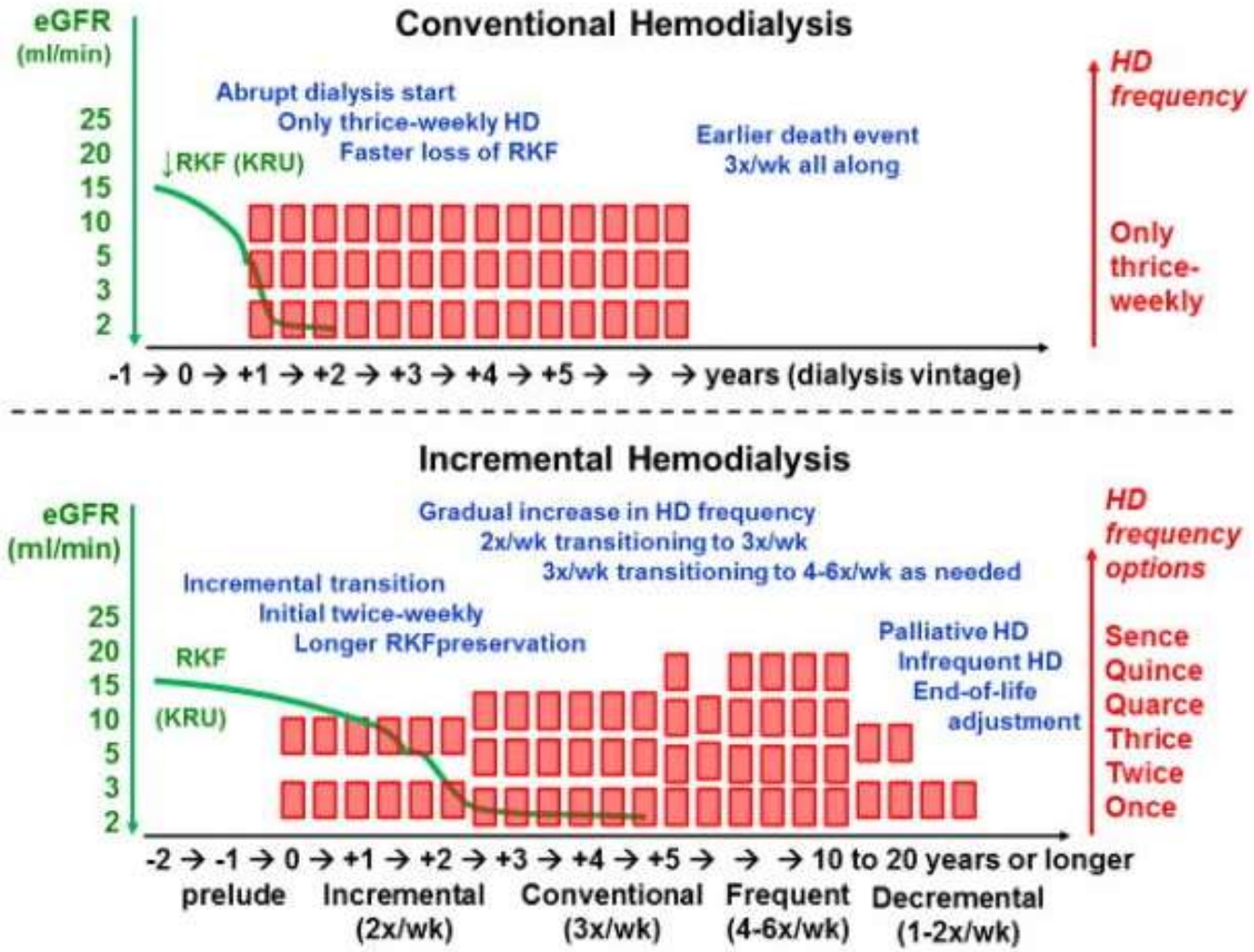
HDF alla luce dello studio Convince: è ormai la metodica di riferimento?

Vincenzo Panichi

PISA

Renal Replacement Therapy and Incremental Hemodialysis for Veterans with Advanced Chronic Kidney Disease

Kamyar Kalantar-Zadeh, Susan T. Crowley, Srinivasan Beddhu, Joline LT Chen, John T Daugirdas,



Semin Dial. 2017 May; 30(3): 251–261.

Emodialisi trisettimanale...le larghe intese

Presupposti fisiologici

Esperienze cliniche

Costi

Logistica

Flessibilità

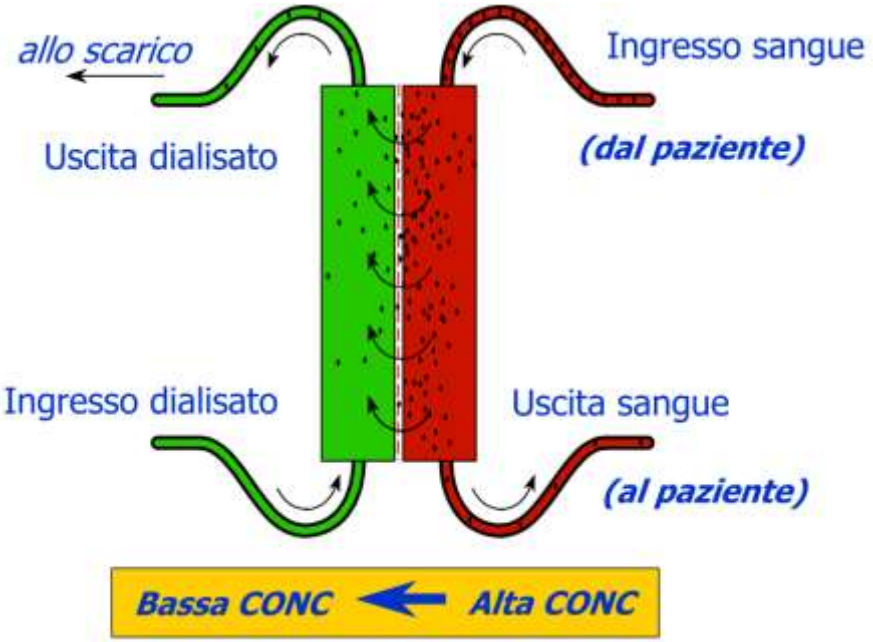
Accettabilità per il paziente

Scribner BH et al., 1960; Held PJ et al., 1983

Principi fisici della dialisi

- **Diffusione**
- **Convezione**
- **Adsorbimento**

EMODIALISI CONVENZIONALE (diffusione)



CARATTERISTICHE

- **Membrana naturale (cellulosica) o sintetica a bassa permeabilità (5 ml/mmHg/mq/ora) e superficie 1,3 mq**
- **Flusso sangue: 300 ml/min**
- **Flusso dialisato: 500 ml/min**
- **Ultrafiltrazione limitata all'incremento ponderale**
- **Durata = 4**

EMODIALISI “High-Flux”

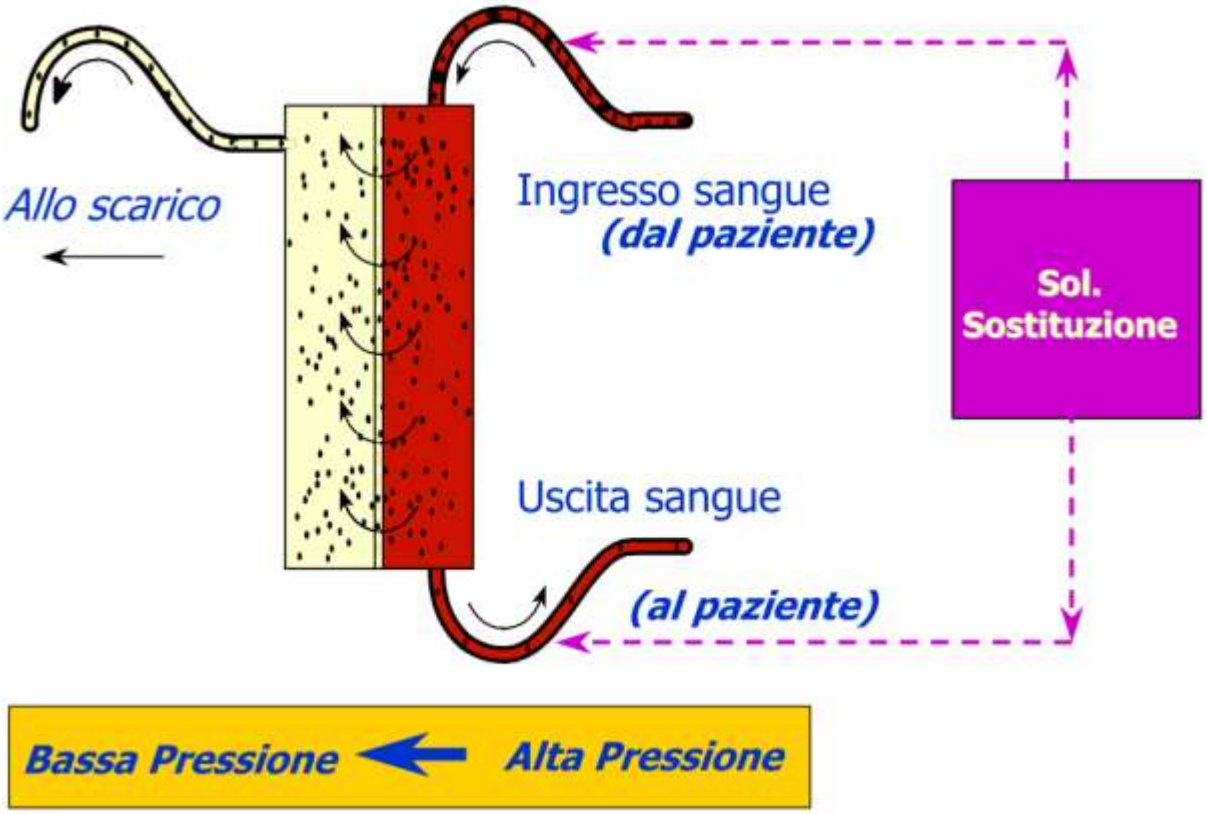
CARATTERISTICHE

- Membrana sintetica ad alta permeabilità diffusiva e convettiva
- (> 20 ml/mmHg/hr) e superficie 1,3- 2,1 mq
- Flusso sangue : 200 - 400 ml/min
- Flusso dialisato: 500-700 ml/min
- Ultrafiltrazione limitata all’incremento ponderale
- Durata = 3 - 4 ore

Principi fisici della dialisi

- Diffusione
- Convezione
- Adsorbimento

EMOFILTRAZIONE (convezione)



Caratteristiche

Membrana sintetica ad alta permeabilità idraulica

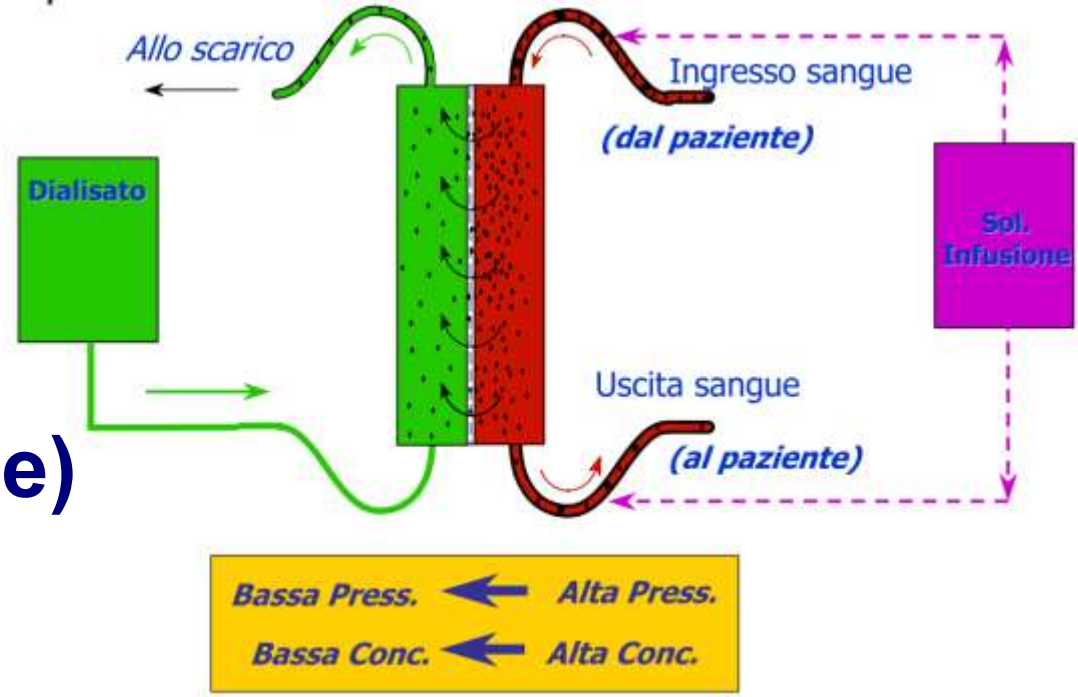
Flusso sangue: 300-400 ml/min

Durata: (in base infusione)

Reinfusione : 30-70 L/seduta = VOLUME DI SOSTITUZIONE

Ultrafiltrazione: reinfusione + decremento peso =VOLUME CONVETTIVO

EMODIAFILTRAZIONE
(diffusione + convezione)



Caratteristiche

Membrana sintetica ad alta permeabilità idraulica

Flusso sangue: 400 ml/min

Flusso dialisato: 500 ml/min

Durata 3- 4 ore

Reinfusione : >20 L/seduta

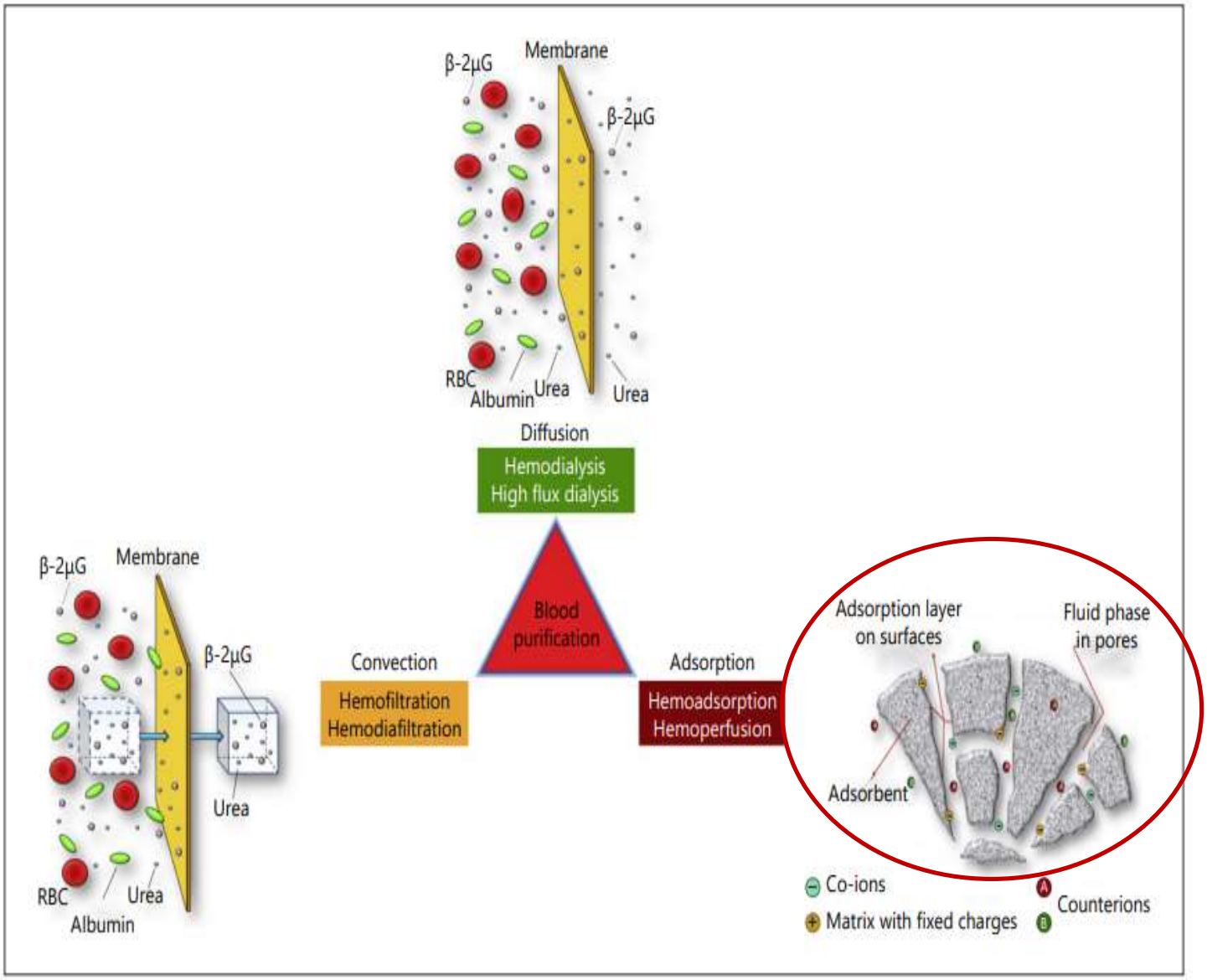
Ultrafiltrazione: reinfusione + decremento peso

I TRATTAMENTI

- Emodialisi (HD): diffusione
- Emofiltrazione (HF): convezione
- Emodiafiltrazione (HDF): diffusione + convezione

Principi fisici della dialisi

- Diffusione
- Convezione
- Adsorbimento


β-2μG
Membrane
β-2μG
RBC
Albumin
Urea
Urea
Diffusion
Hemodialysis
High flux dialysis
Blood purification
Convection
Hemofiltration
Hemodiafiltration
Adsorption
Hemoadsorption
Hemoperfusion
β-2μG
Membrane
β-2μG
Urea
RBC
Albumin
Urea
Adsorption layer on surfaces
Fluid phase in pores
Adsorbent
Co-ions
Matrix with fixed charges
Counterions

Adsorption: what techniques are available?

Adsorption capacities of several membranes

Hemodiafiltration with endogenous reinfusion or HFR

Hemodialysis coupled with an adsorbent cartridge

Received: 1 July 2020 / Accepted: 4 February 2021

Classification of uremic toxins

Small water soluble solutes	Protein-bound solutes	Middle molecules
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

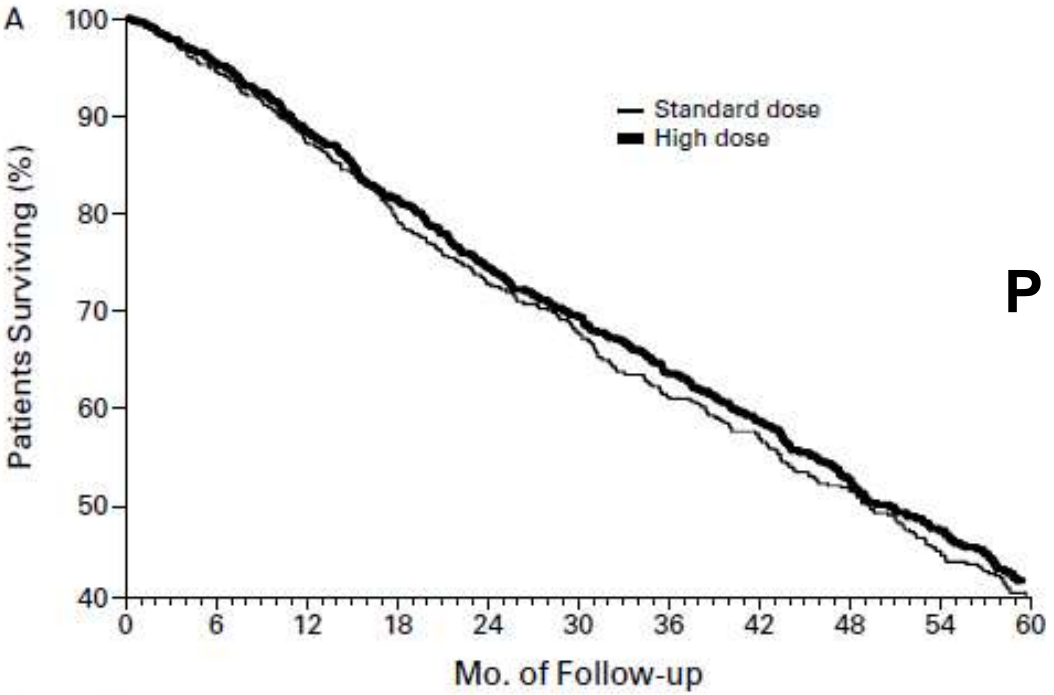
Vanholder R. et al New insights in uremic toxins. *Kidney Int*, 2003, 63; 84: S6–S10

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*

HEMO study

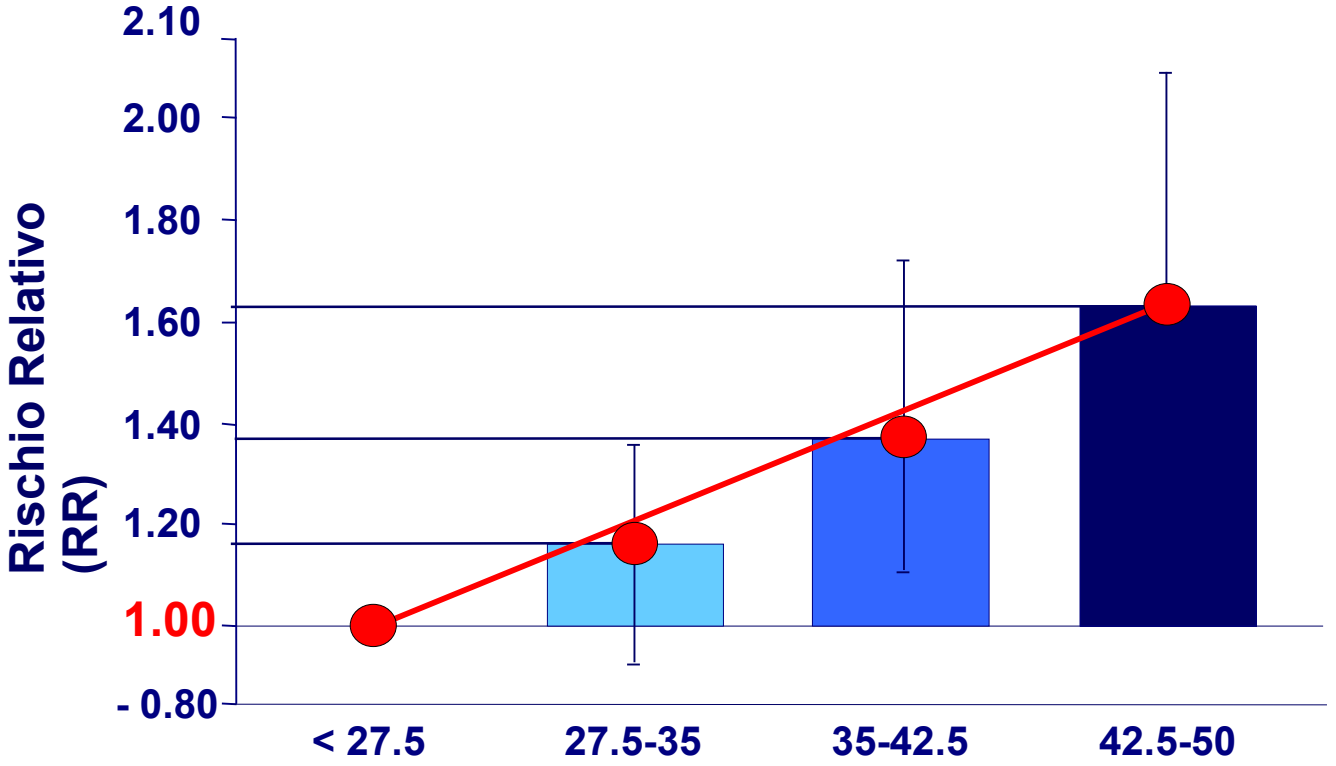


P = 0.53

NO. AT RISK

Standard dose	854	759	630	524	451	382	315	253	197	149
High dose	857	753	637	538	470	399	327	266	219	166

Alti livelli di β2-m predicono la mortalità nei pazienti in emodialisi



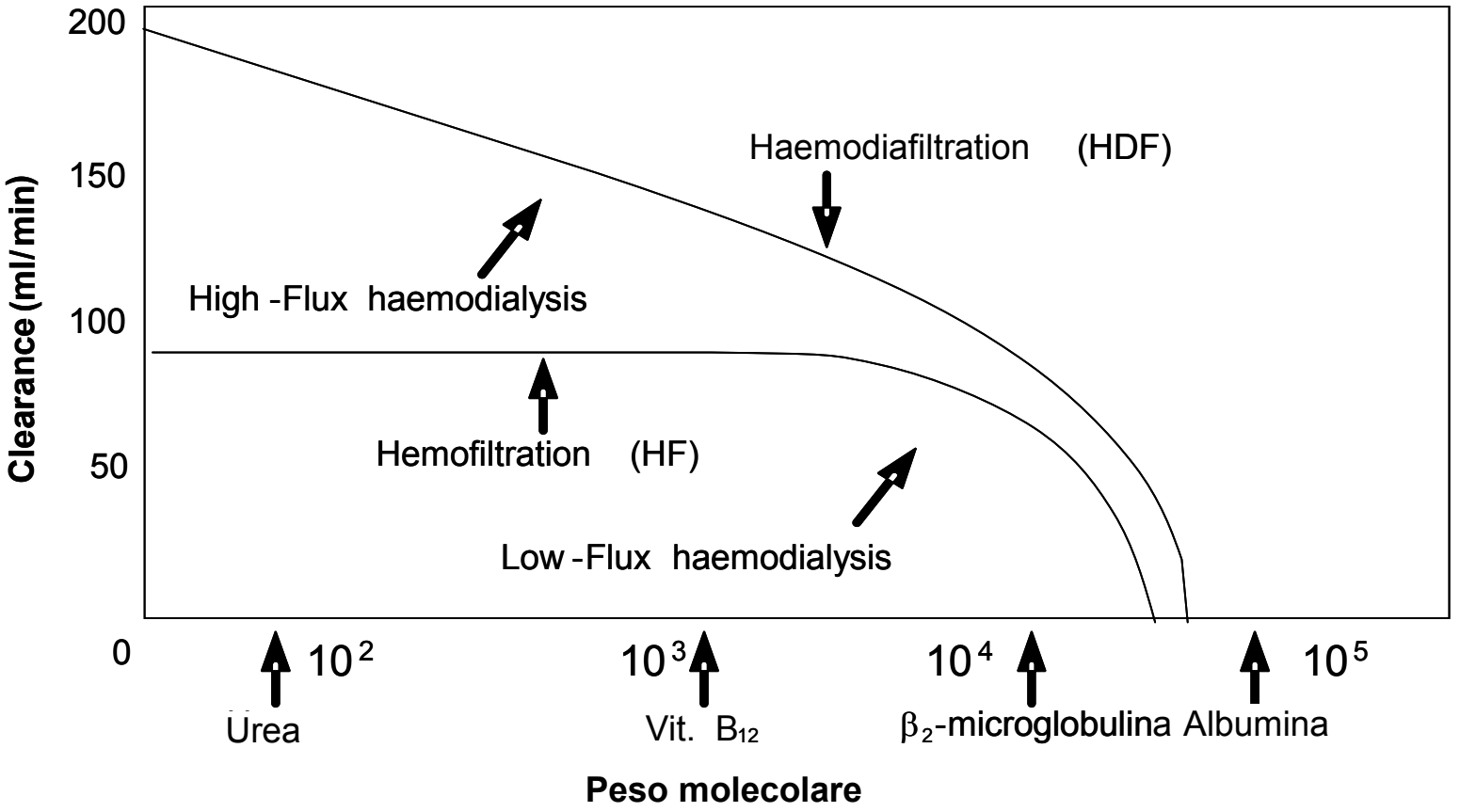
HEMO study

***n* = 1,704 pz.**

Rischio relativo = 1.11 ogni 10 *mg/L* di incremento della ß2-m (1.05 - 1.19)

Cheung AK et al, *J Am Soc Nephrol 2006; 17: 546-55*

Clearance e peso molecolare in diverse tecniche dialitiche



Ledebo I. Principles and practice of hemofiltration and hemodiafiltration. *Artif Organs 1998; 22 (1): 20-25*

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

Global prevalent use, trends and practices in haemodiafiltration

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

ndt
Nephrology Dialysis Transplantation

In brief, haemodialysis has moved from:

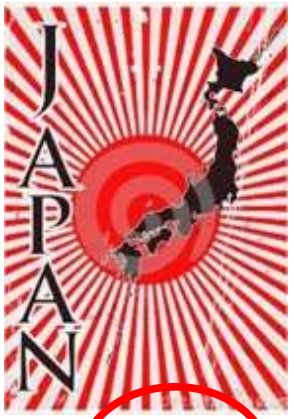
In brief, haemodialysis has moved from:

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 .

Online HDF in the World

~ 26%



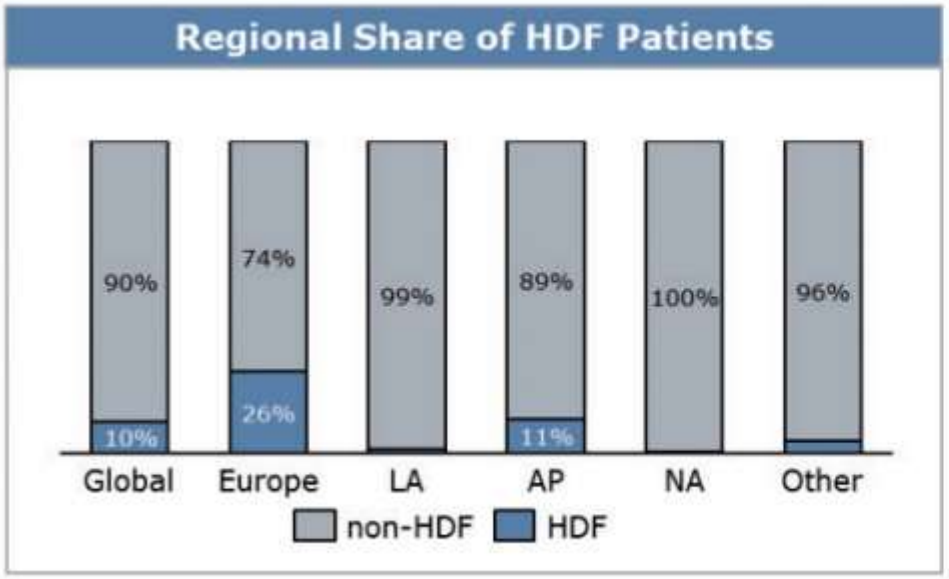
~ 11%

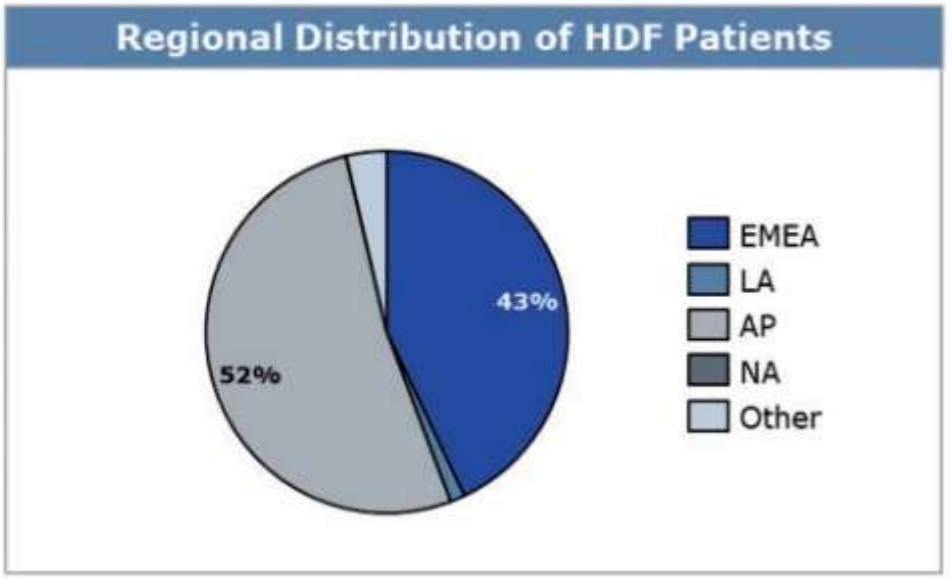
Virtually 0%

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

Global prevalent use, trends and practices in haemodiafiltration

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





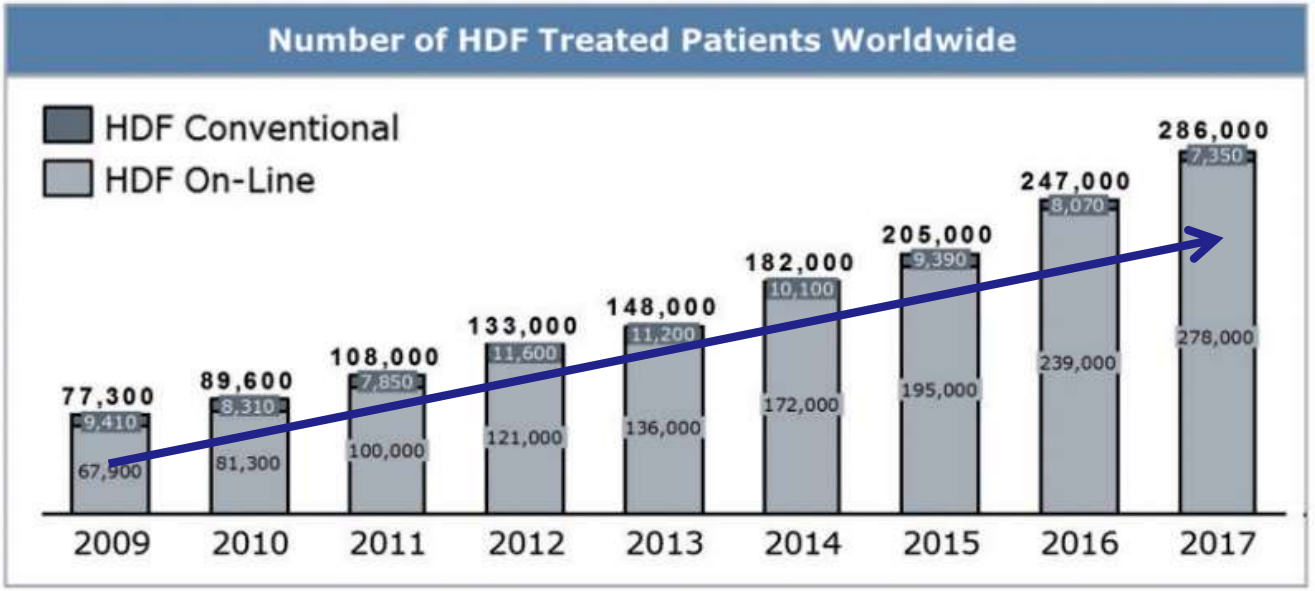
Abbreviation: LA: Latin America; AP: Asia Pacific; NA: North America.

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

Global prevalent use, trends and practices in haemodiafiltration

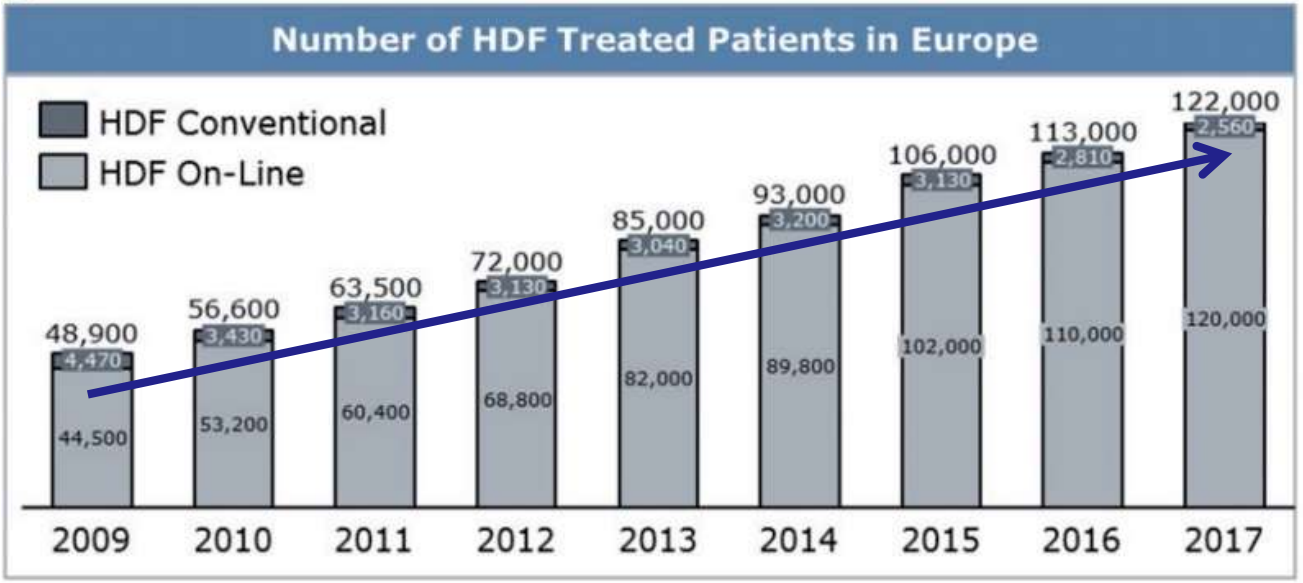
Bernard Canaud[1,2], Katrin Köhler[1], Jan-Michael Sichart[3] and Stefan Möller[3]

ndt
Nephrology Dialysis Transplantation

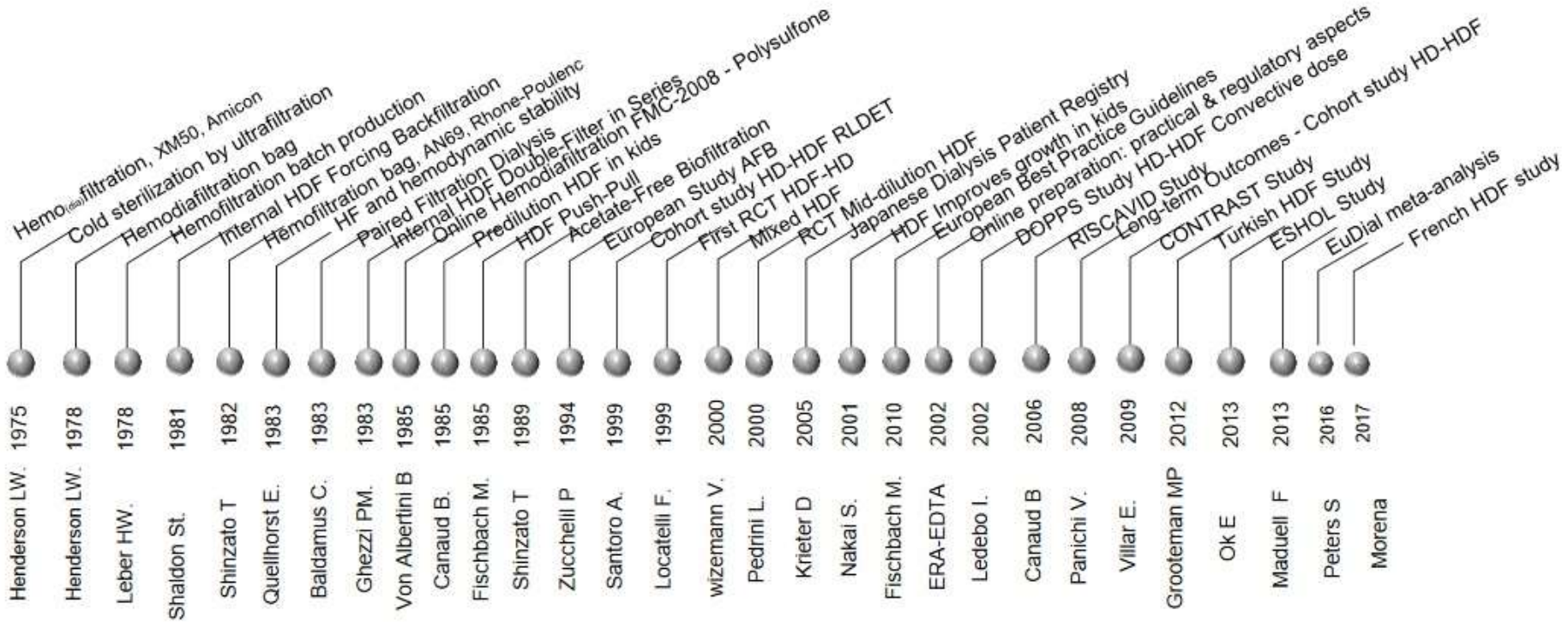


WORLD

EUROPE



Major milestones in online HDF development



Adapted from figure by Bernard Canaud

UMC Utrecht
Center for Circulatory Health

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 clinical trial

Kidney Int 2017

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, Nîmes, 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
Clinical Kidney Journal, 2015, vol. 8, no. 4, 368–373
doi: 10.1093/ckj/sfv040
Advance Access Publication Date: 10 June 2015
CKJ Review

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.

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

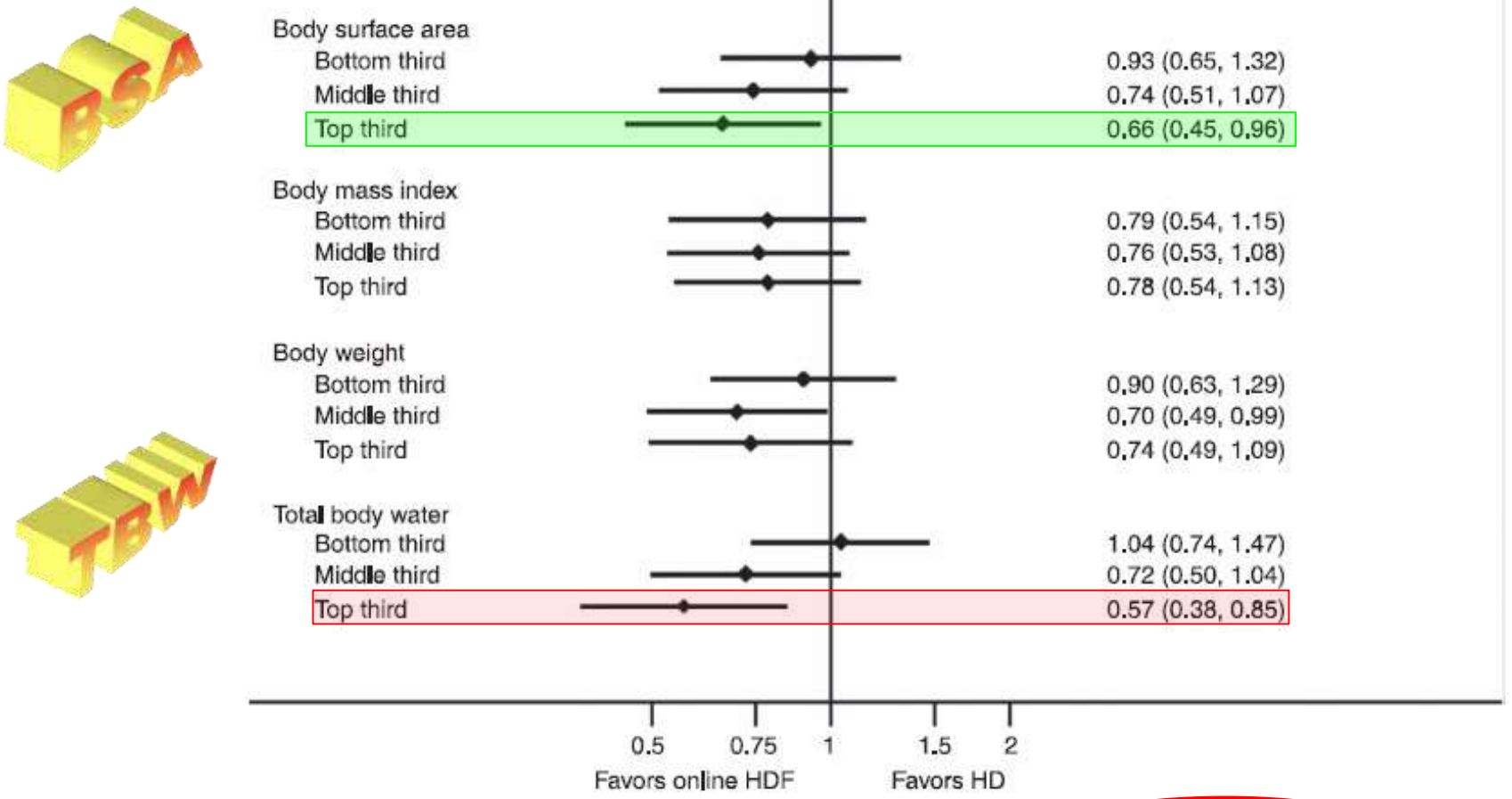


Figure 2 | Hazard ratios (HRs; boxes) and 95% confidence intervals (CI; bars) for cardiovascular mortality in patients receiving online hemodiafiltration versus hemodialysis by convection volume, using different methods to standardize convection volume.

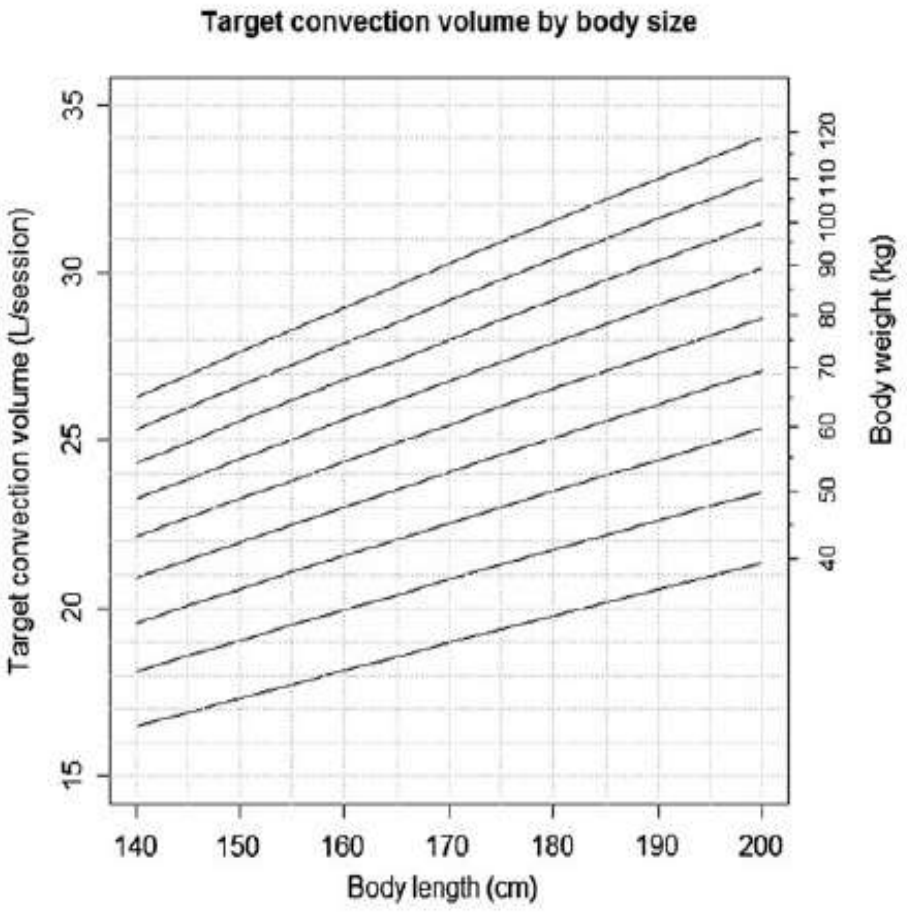
NDT Advance Access published October 22, 2015

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.

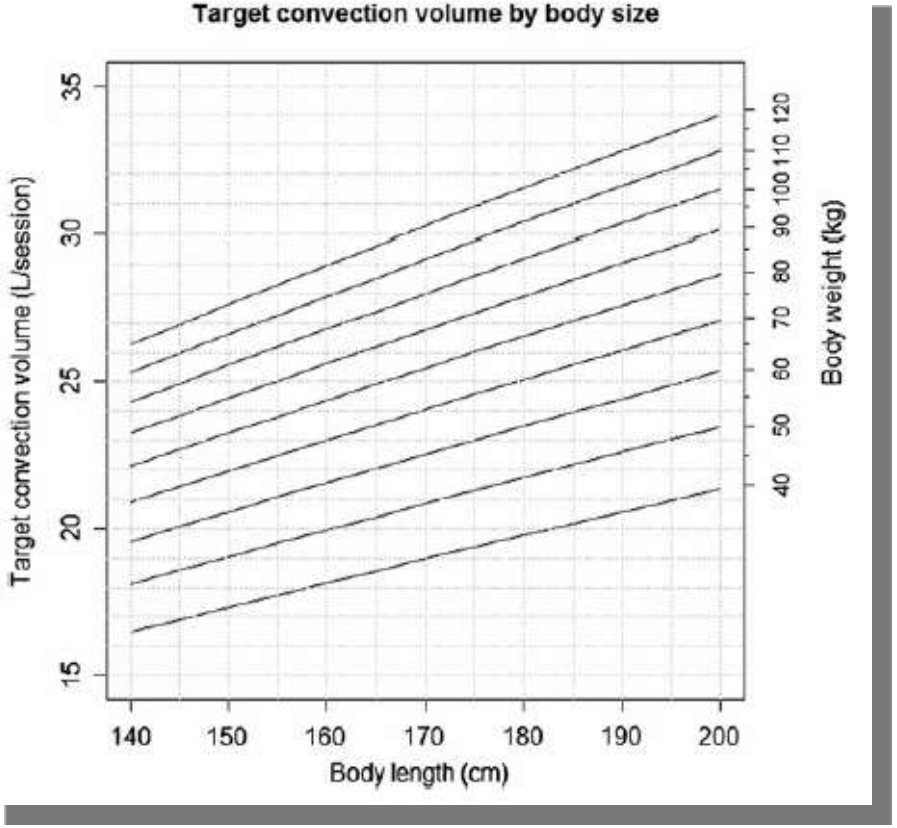
BSA was calculated using Formula Gehan and George as recommended by the European Best Practice Guidelines **[BSA (m2) = 0.0235 × baseline height (cm) 0.42246 × baseline weight (kg) 0.51456]**

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

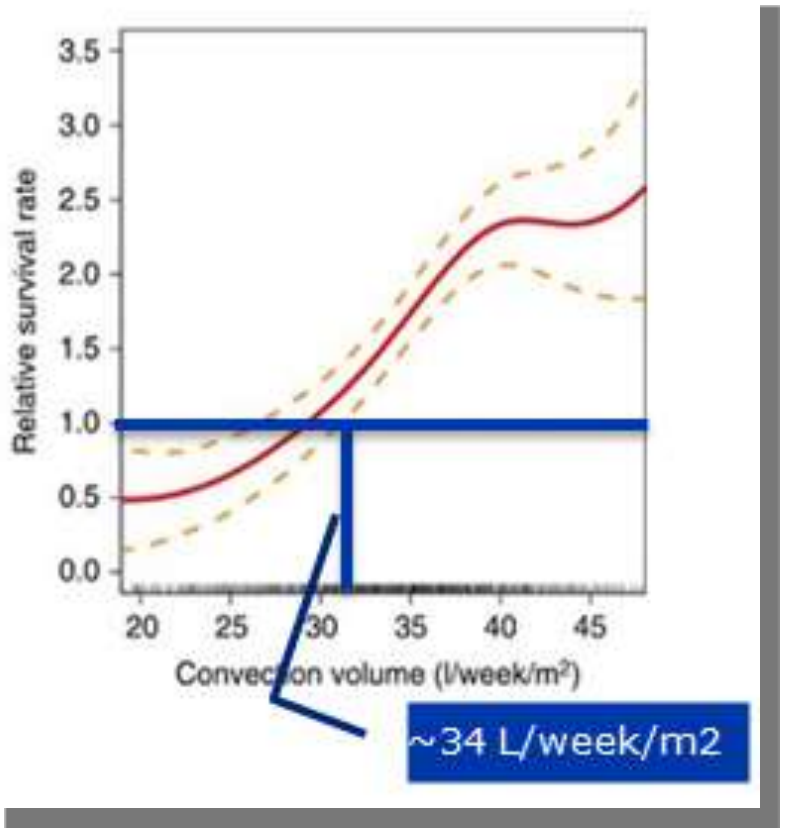
23 l / seduta / 1,73m²



CANAUD B et al, 2015

>34 l / settimana / m²

>11 l / seduta / m²



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ndt
Nephrology Dialysis Transplantation

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],

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

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

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

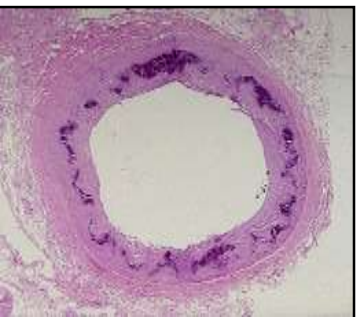
Online hemodiafiltration and mortality risk in end-stage renal disease patients: A critical appraisal of current evidence

Table 2. Advantages (observed benefits) of post-dilution hemodiafiltration

Morbidity
1. Fewer episodes of intradialytic hypotension
2. Fewer/delayed clinical manifestations of AB amyloidosis
3. Improved nutritional status and inflammation
4. Better correction of renal anemia
5. Improved quality of life
6. Growth of pediatric end-stage renal disease patients
Mortality
1. Reduced all-cause mortality
2. Reduced cause-specific mortality (cardiac death)

IL-10, IL-6, and TNF-α: Central factors in the altered cytokine network of uremia—The good, the bad, and the ugly

PETER STENVINKEL, MARKUS KETTELER, RICHARD J. JOHNSON, BENGT LINDHOLM, ROBERTO PECOITS-FILHO, MIGUEL RIELLA, OLOF HEIMBÜRGER, TOMMY CEDERHOLM, and MATTHIAS GIRNDT



Media Calcification

Uremic milieu

Cytokine production

TNF-α (+) IL-6 (+) IL-10 (–)

↑ Erythropoietin resistance

↑ Bone remodeling

↑ Insulin resistance

↑ Muscle catabolism

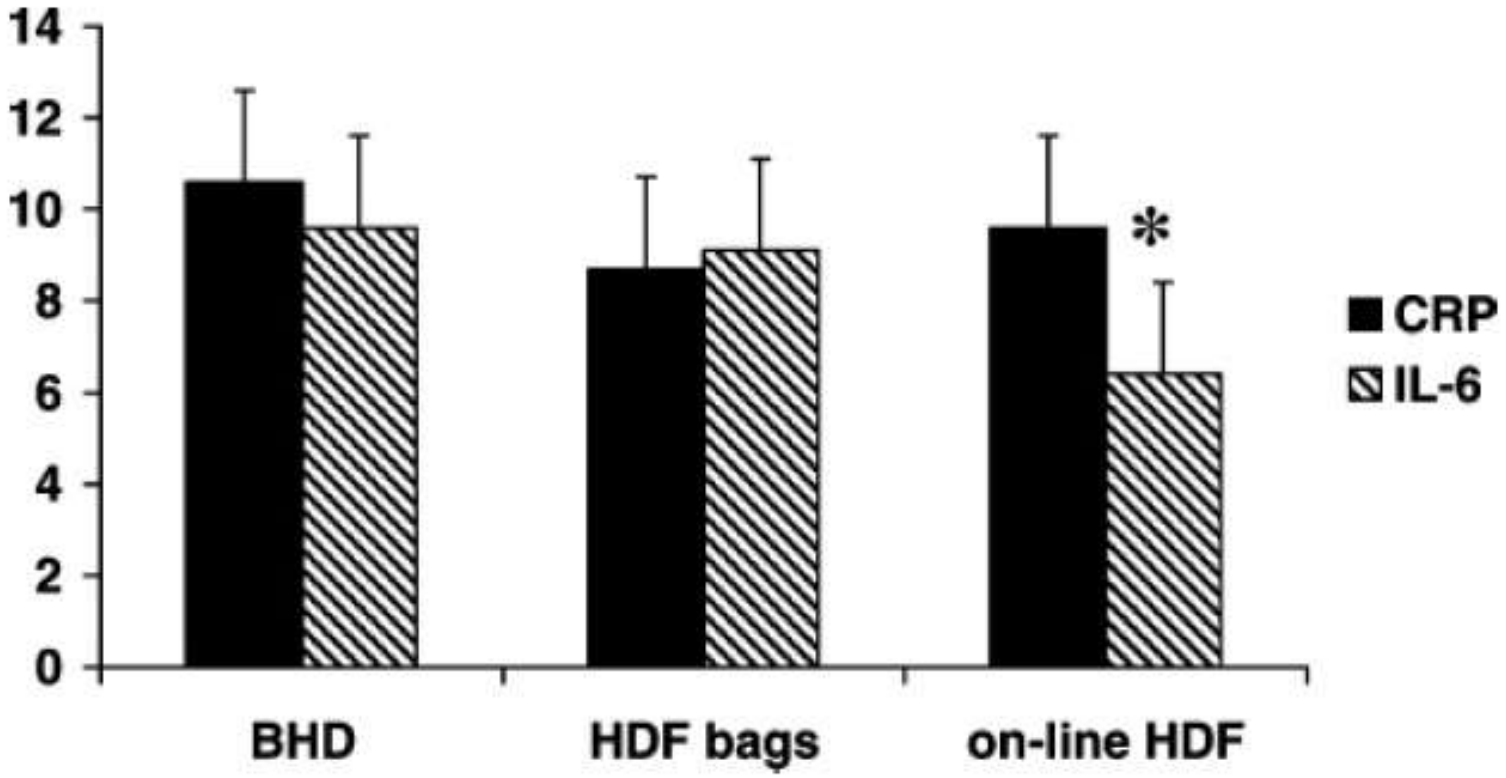
↑ Acute phase reactants
↓ Fetuin-A

↑ Adipocytokine production

↓ Appetite

↑ Endothelial dysfunction
↑ Monocyte adhesion
↑ Smooth muscle cell proliferation
↑ Oxidative stress
↑ Vascular calcification

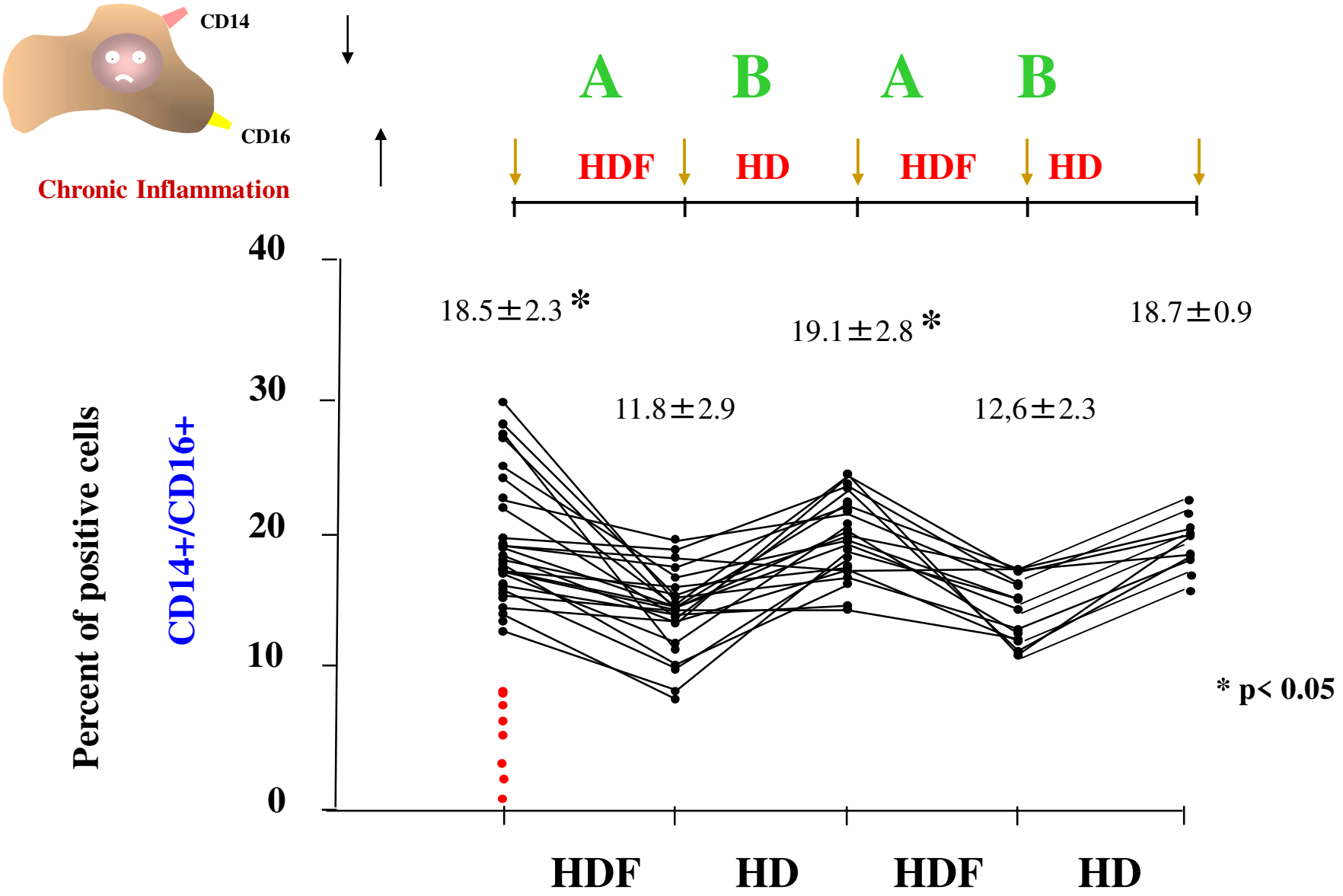
Effects on chronic inflammation



RISCAVID Study

Panichi V et al. Nephrol Dial Transplant. 2008; 23:2337-2343

CD14+/CD16+ monocytes in HD vs. HDF

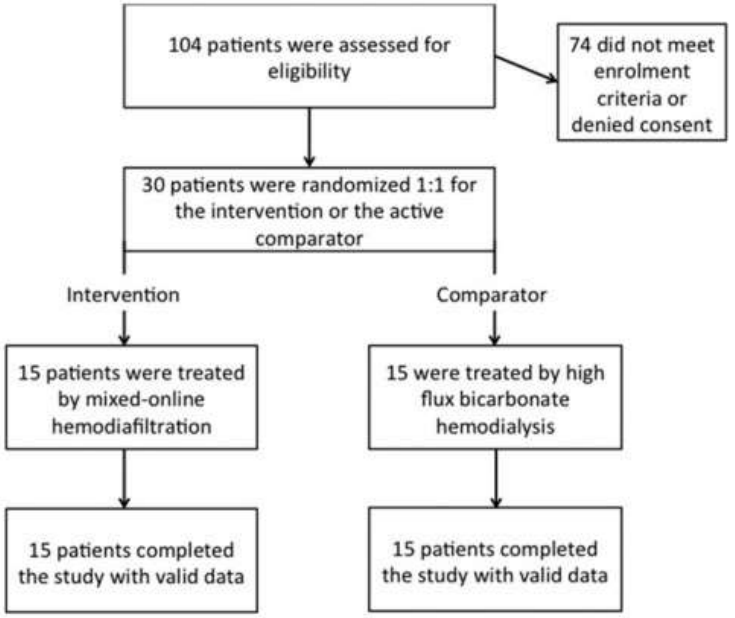


Carracedo J et al, J Am Soc Nephrol 17: 2315-2321, 2006

Online Hemodiafiltration Inhibits Inflammation-Related Endothelial Dysfunction and Vascular Calcification of Uremic Patients Modulating miR-223 Expression in Plasma Extracellular Vesicles

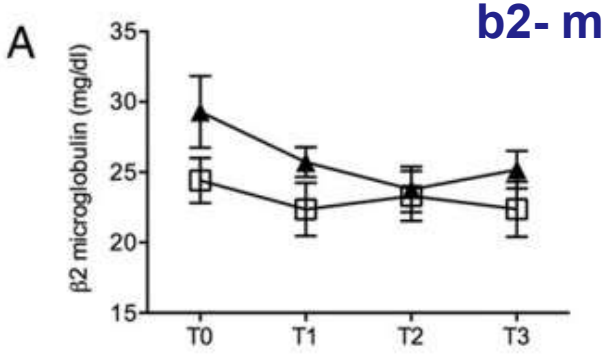
The Journal of Immunology

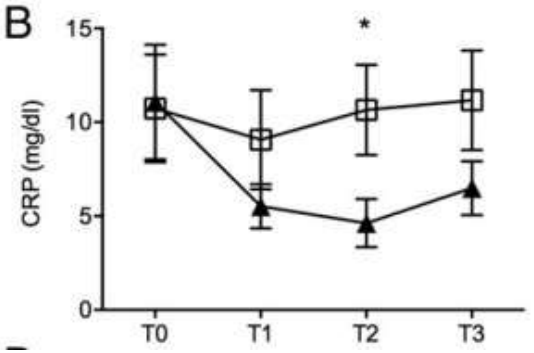
Claudia Cavallari,*,[1] Sergio Dellepiane,†,[1] Valentina Fonsato,* Davide Medica,† Marita Marengo,‡ Massimiliano Migliori,§ Alessandro D. Quercia,¶,‖ Adriana Pitino,* Marco Formica,‡ Vincenzo Panichi,§ Stefano Maffei,† Luigi Biancone,† Emanuele Gatti,# Ciro Tetta,** Giovanni Camussi,† and Vincenzo Cantaluppi¶,‖



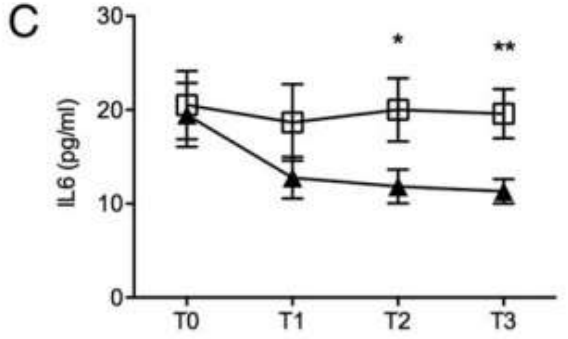
Study flowchart

b2- microglobulin





CRP

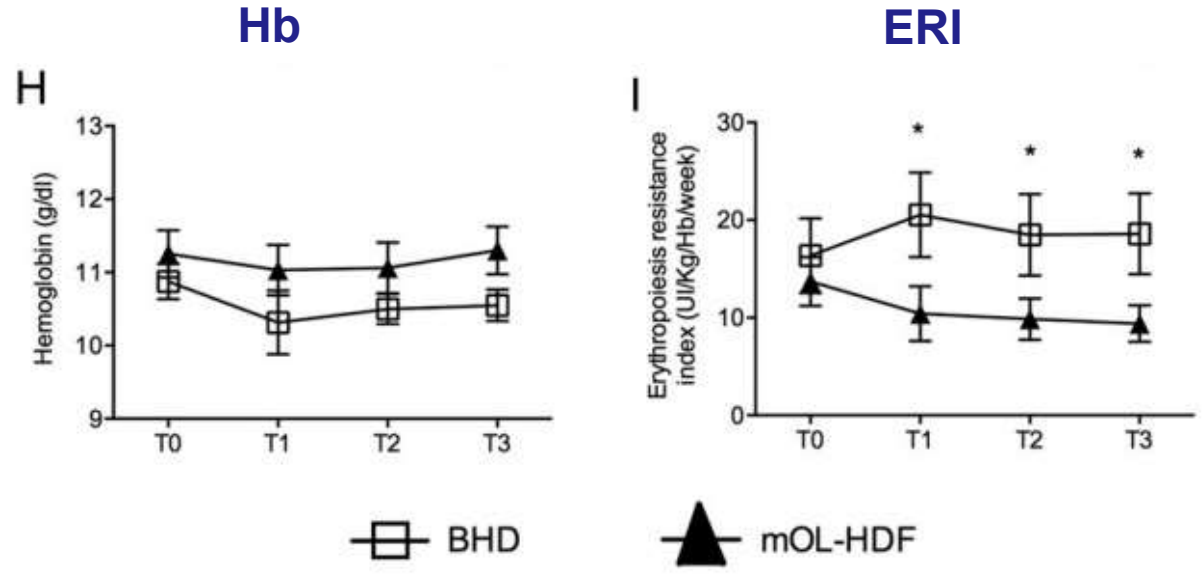


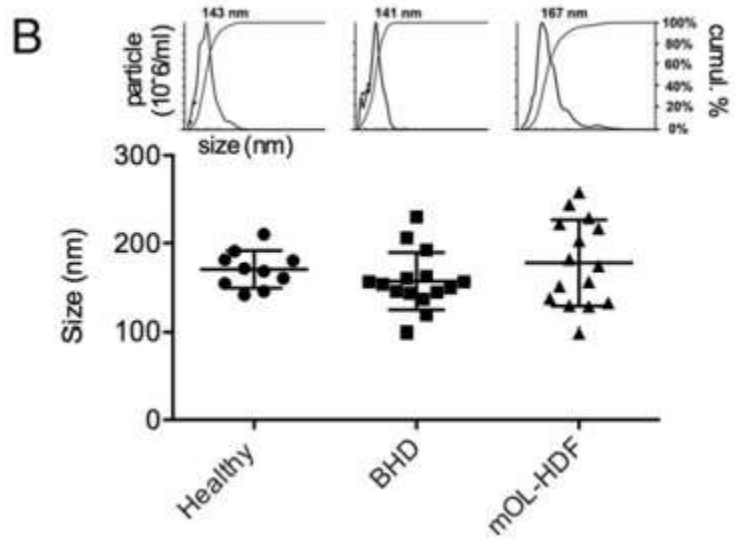
IL-6

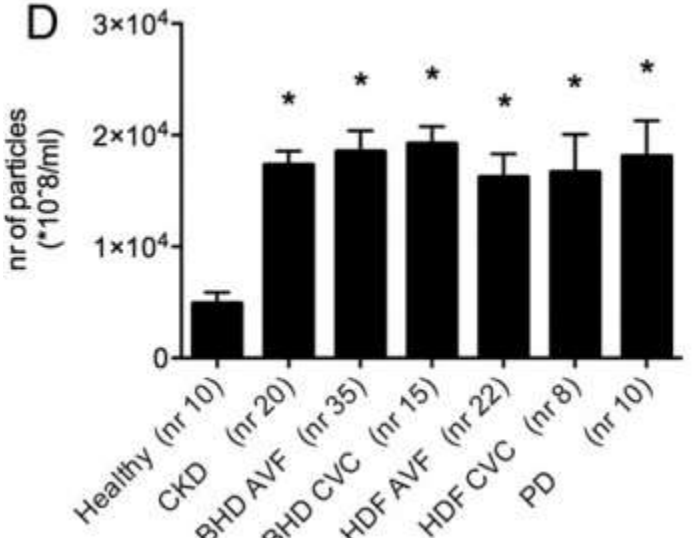
Online Hemodiafiltration Inhibits Inflammation-Related Endothelial Dysfunction and Vascular Calcification of Uremic Patients Modulating miR-223 Expression in Plasma Extracellular Vesicles

Claudia Cavallari,*[,1] Sergio Dellepiane,[†,1] Valentina Fonsato,* Davide Medica,[†] Marita Marengo,[‡] Massimiliano Migliori,[§] Alessandro D. Quercia,[¶,‖] Adriana Pitino,* Marco Formica,[‡] Vincenzo Panichi,[§] Stefano Maffei,[†] Luigi Biancone,[†] Emanuele Gatti,[#] Ciro Tetta,** Giovanni Camussi,[†] and Vincenzo Cantaluppi[¶,‖]

The Journal of Immunology







Review Article

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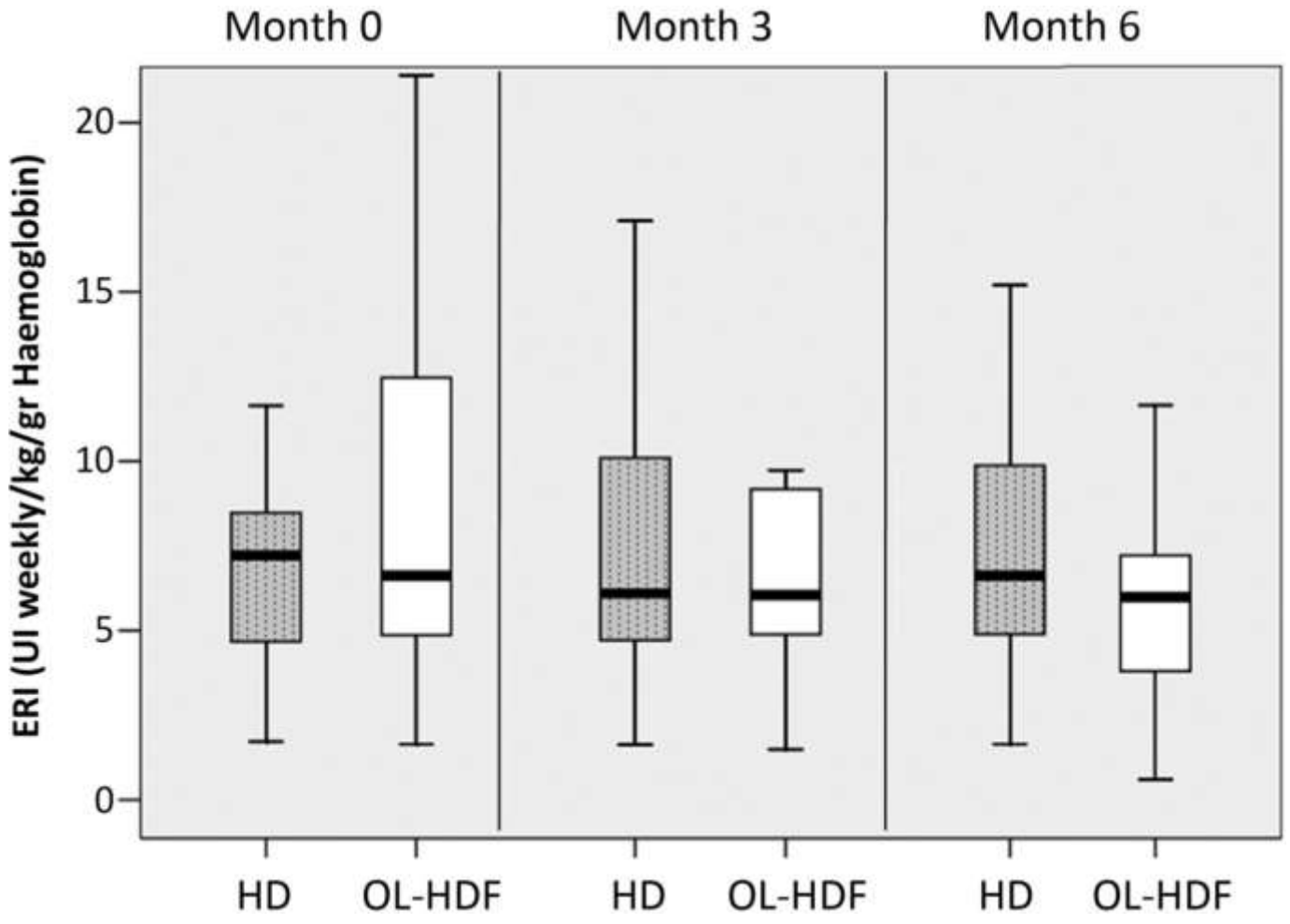
Nephrol Dial Transplant (2015) 30: 682–689
doi: 10.1093/ndt/gfu345
Advance Access publication 10 November 2014

High-volume online haemodiafiltration improves erythropoiesis-stimulating agent (ESA) resistance in comparison with low-flux bicarbonate dialysis: results of the REDERT study

Vincenzo Panichi[1], Alessia Scatena[1], Alberto Rosati[2], Riccardo Giusti[2], Giuseppe Ferro[3], Erasmo Malagnino[2], Alessandro Capitanini[4], Adriano Piluso[4], Paolo Conti[5], Giada Bernabini[5], Massimiliano Migliori[1], David Caiani[5], Ciro Tetta[6], Aldo Casani[7], Giancarlo Betti[7] and Francesco Pizzarelli[3]



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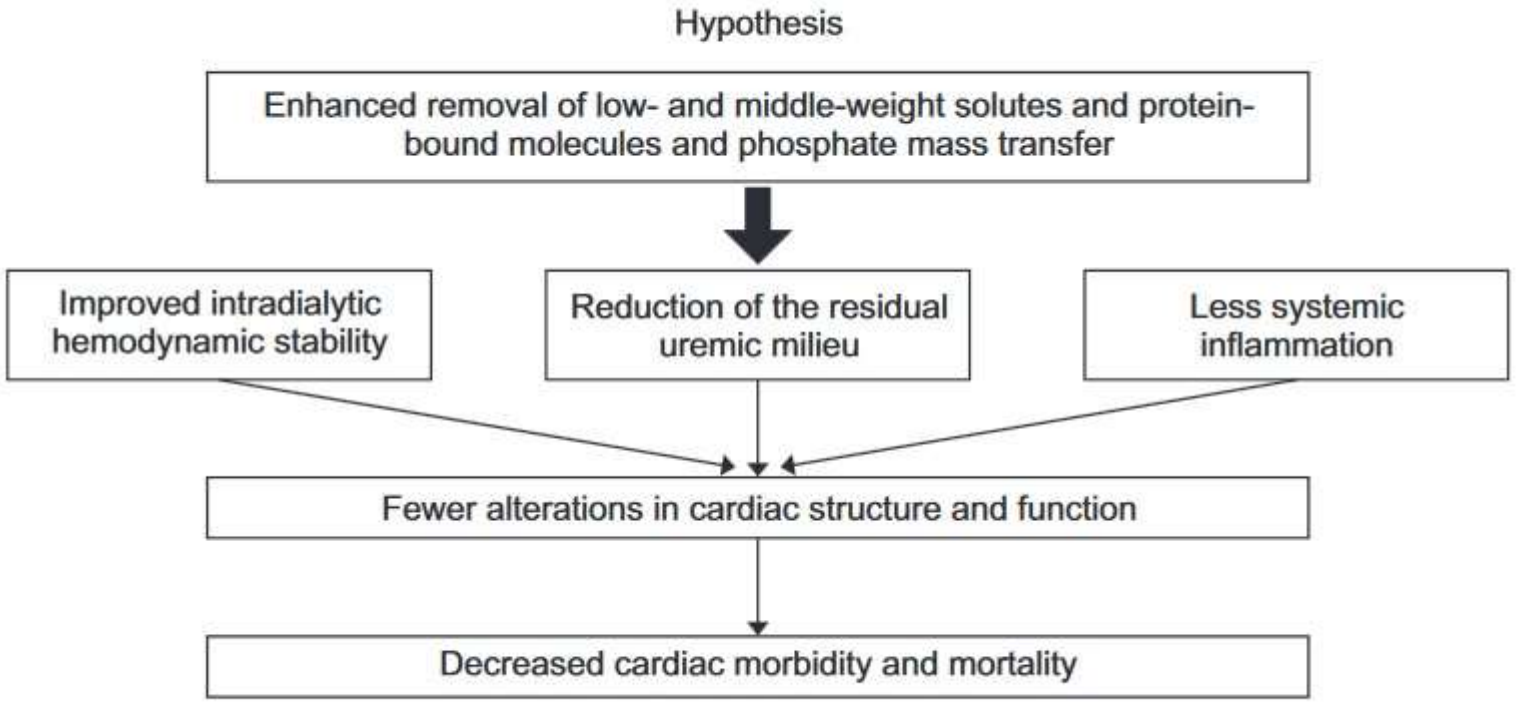
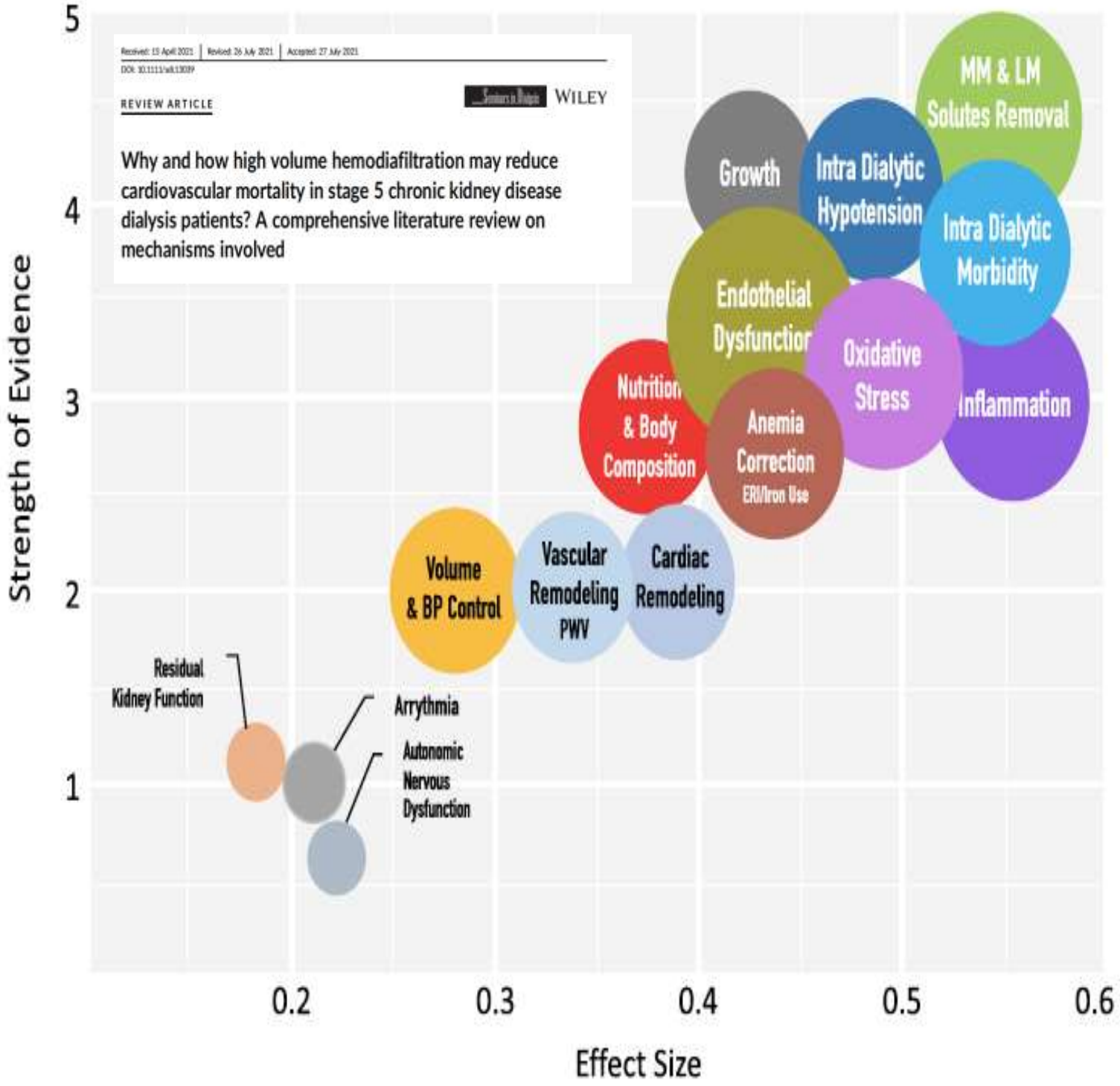



Received: 13 April 2021 | Revised: 26 July 2021 | Accepted: 27 July 2021
DOI: 10.1111/wll.13039
REVIEW ARTICLE
WILEY
Why and how high volume hemodiafiltration may reduce cardiovascular mortality in stage 5 chronic kidney disease dialysis patients? A comprehensive literature review on mechanisms involved
MM & LM Solutes Removal
Growth
Intra Dialytic Hypotension
Intra Dialytic Morbidity
Endothelial Dysfunction
Oxidative Stress
Nutrition & Body Composition
Anemia Correction
ERI/Iron Use
Inflammation
Volume & BP Control
Vascular Remodeling
PWV
Cardiac Remodeling
Residual Kidney Function
Arrythmia
Autonomic Nervous Dysfunction
Strength of Evidence
Effect Size
5
4
3
2
1
0.2
0.3
0.4
0.5
0.6

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

Nephrol Dial Transplant (2016) 31: 978–984
doi: 10.1093/ndt/gfv349
Advance Access publication 22 October 2015

Original Articles

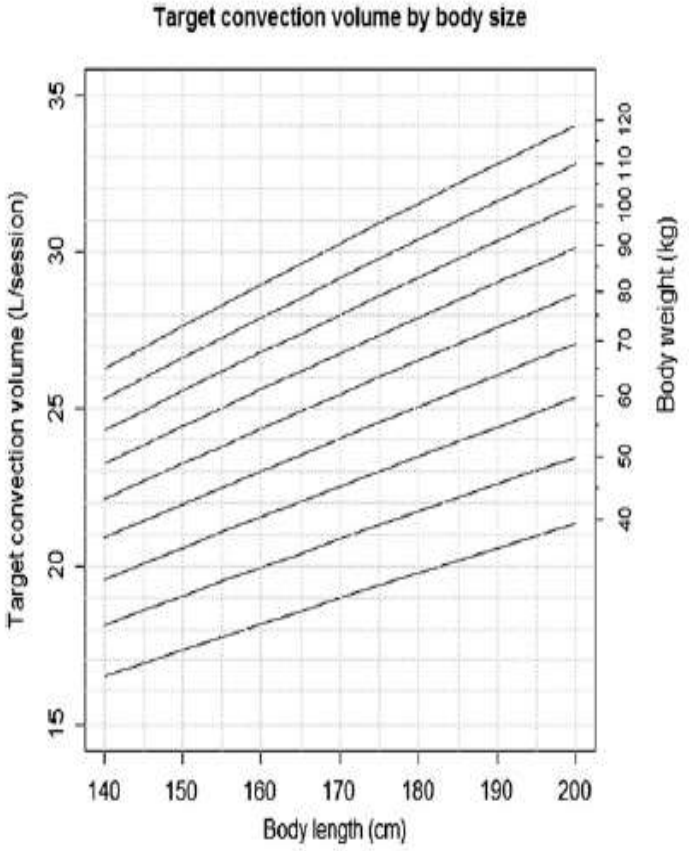


Table 3. HR and 95% CIs for all-cause mortality and cause-specific mortality by delivered BSA-standardized convection volume in litres per 1.73 m^2 per treatment with standard HD as a reference

Cause	Online HDF: BSA-adjusted convection volume (L/session)		
	<19	19–23	>23
All-causes			
Unadjusted	0.91 (0.74; 1.13)	0.88 (0.72; 1.09)	0.73 (0.59; 0.91)
Adjusted	0.83 (0.66; 1.03)	0.93 (0.75; 1.16)	0.78 (0
Cardiovascular			
Unadjusted	1.00 (0.71; 1.40)	0.71 (0.50; 1.01)	0.69 (0.48; 0.98)
Adjusted	0.92 (0.65; 1.30)	0.71 (0.49; 1.03)	0.69 (0
Infections			
Unadjusted	1.50 (0.93; 2.41)	0.96 (0.56; 1.65)	0.56 (0.30; 1.08)
Adjusted	1.50 (0.92; 2.46)	0.97 (0.54; 1.74)	0.62 (0.32; 1.19)
Sudden death			
Unadjusted	1.24 (0.80; 1.91)	0.91 (0.57; 1.47)	0.60 (0.35; 1.03)
Adjusted	1.09 (0.69; 1.74)	1.04 (0.63; 1.70)	0.69 (0.39; 1.20)

- 22%

- 31%

Values are HRs and 95% CI.
Adjusted for age, sex, albumin, creatinine, history of cardiovascular diseases and history of diabetes.

Cochrane Library

Cochrane Database of Systematic Reviews

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.

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**

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

UMC Utrecht
Center for Circulatory Health

CONVINCE STUDY

CONVINCE in the context of existing evidence on haemodiafiltration

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

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*** *…..This occurs when the* ***variables that predispose selection in the dosage of the intervention are also related to outcomes***. The patient and treatment characteristics that are associated with achieving higher convective volumes (e.g. less comorbidities, vascular access, blood flow) are also **independently associated with mortality and may therefore explain the beneficial effects reported for stratification of convection volume**

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]

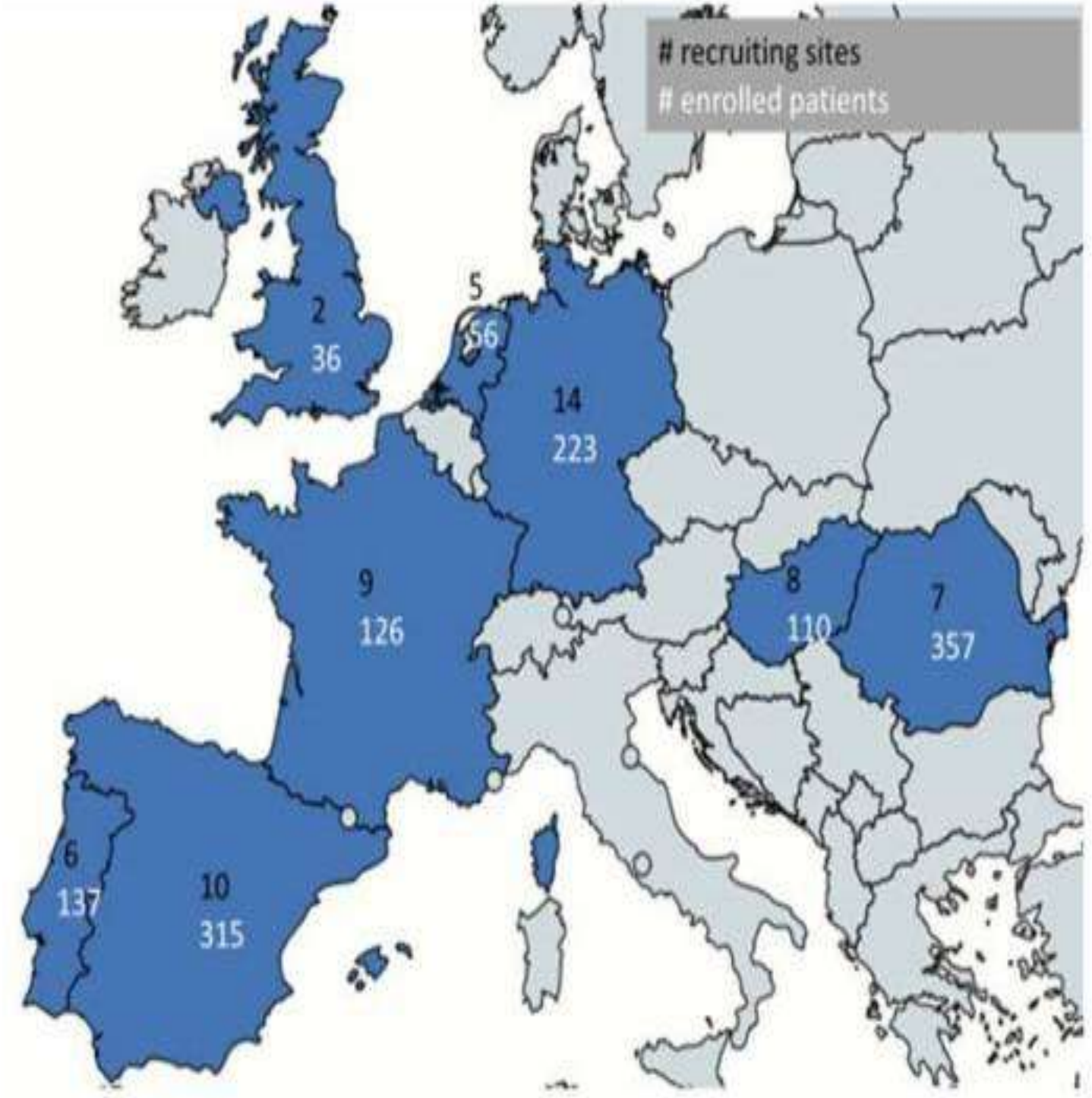
Strengths and limitations of this study

- 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.


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

Benefits and harms of high dose haemodiafiltration versus high flux haemodialysis (CONVINCE) trial protocol

BMJ Blankestijn PJ, *et al. BMJ Open* 2020;**10**:e033228. doi:10.1136/bmjopen-2019-033228

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.

….on the 2.5-year mortality rate, and an estimated average follow-up of approximately 2.5 years, 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 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

Table 3. Risk of bias of the four randomized controlled trials included in the individual patient data meta-analysis and the two ongoing trials.

	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting
CONTRAST[a]	+	?	−	+	+	+
ESHOL[a]	+	?	−	−	−	+
French study	+	+	−	?	+	+
Turkish HDF 2013[a]	?	?	−	−	−	+
CONVINCE	+ (A block randomization scheme, stratified by centre)	+ (Allocation to high-flux HD and high-dose HDF will be concealed by central randomization)	− (Open label)	+ (Objective outcomes or self-reported outcomes)	+ (If a participant drops out e.g. due to kidney transplantation, switching to another dialysis modality or transferring out of the participating centre, effort will be made to collect information on his/her vital status until the end of the study follow-up)	+ (Netherlands National Trial Register—NTR 7138)
H4RT	+ (Randomization will utilize the existing remote automated computer randomization application)	+ (Randomization will be done using the Bristol Randomised Trials Collaboration Randomization System, which provides a secure service to generate allocations)	− (Open label)	+ (Objective outcomes or self-reported outcomes)	+ (Adherence to the protocol will be monitored through UK Renal Registry treatment modality returns and contact with dialysis units throughout the follow-up. As the UK Renal Registry follows all patients on renal replacement therapy in the UK, patients should not be lost to follow-up unless they move to another country)	+ (A priori developed protocol)

+: low risk of bias, ?: unclear risk of bias, −: high risk of bias, [a]as assessed by Nistor *et al.* (2015).

Quali limiti agli studi? Saranno superati?

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

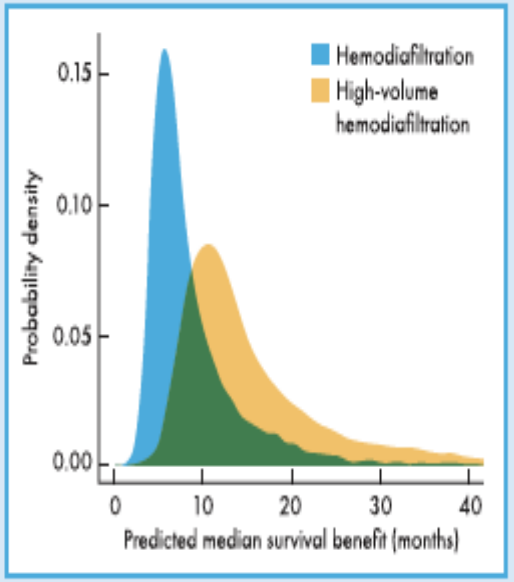
Royston-Parmar model for prediction of absolute treatment effect

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.

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

CONVINCE study

ORIGINAL ARTICLE

Effect of Hemodiafiltration or Hemodialysis on Mortality in Kidney Failure

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2023

Aims

Objectives	Description
Primary Objective	to **compare HDF** when delivered consistently in high-dose, with high-flux **HD** treatment in terms of **all-cause mortality**.
Secondary Objectives	1. Compare treatments in terms of cause specific morbidity and mortality. 2. Assess **PRO-s** to capture patient perspectives and compare between treatments. 3. Assess cost effectiveness of high-dose HDF.

Methods

Multicentre, multinational

EU-funded; Horizon 2020 grant no 754803

Registeration: International Clinical Trial Registry Platform, NTR 7138

CRO: Julius Clinical, the Netherlands (www.juliusclinical.org)

Inclusion/exclusion criteria: pragmatic, except for

- likelihood of achieving the 23L convection volume (= total ultrafiltration volume, i.e. sum of substitution volume and net UF volume to achieve dry weight)
- ability to complete the patient reported outcome assessments

Outcomes: ACM; cause-specific death; patient reported outcomes

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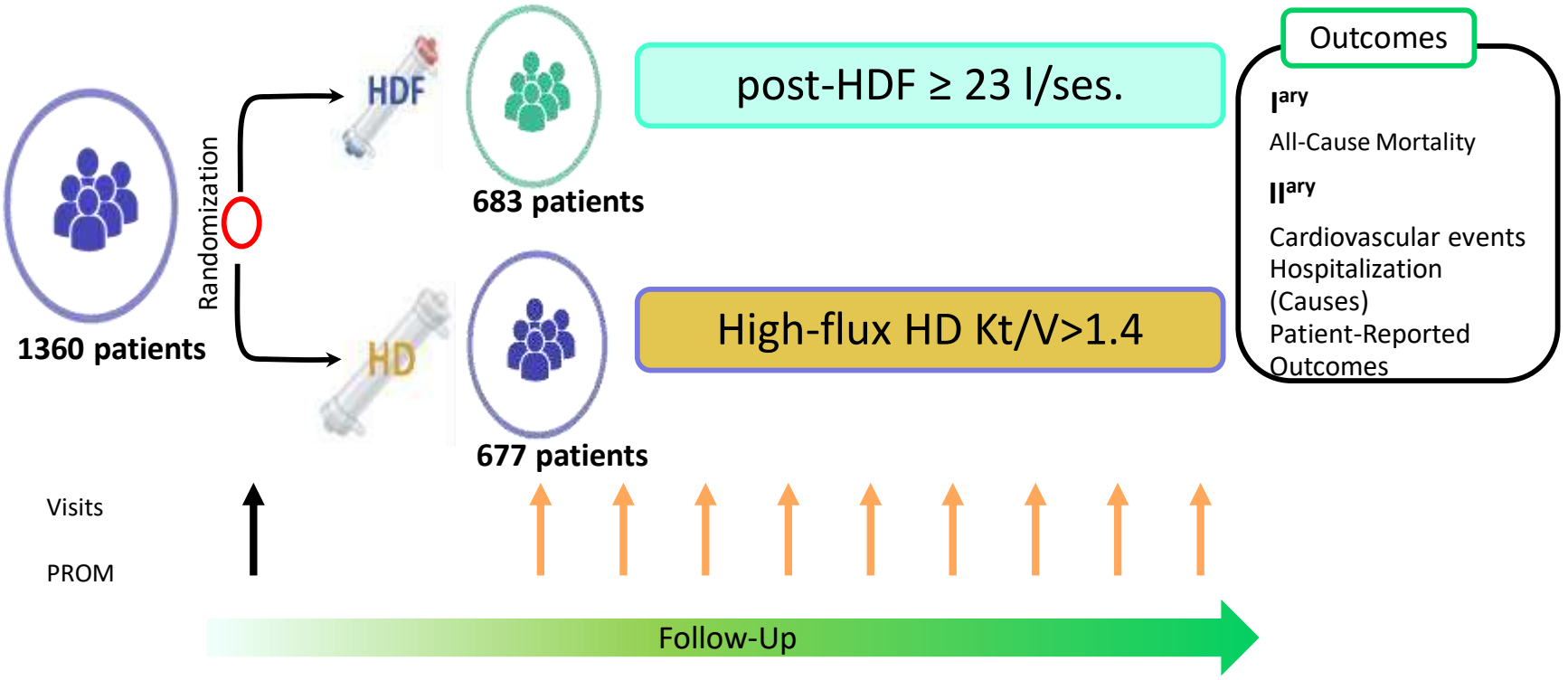

1360 patients
Randomization
HDF
683 patients
post-HDF ≥ 23 l/ses.
HD
677 patients
High-flux HD Kt/V>1.4
Outcomes
I^ary
All-Cause Mortality
II^ary
Cardiovascular events
Hospitalization
(Causes)
Patient-Reported
Outcomes
Visits
PROM
Follow-Up

Results: baseline data

Characteristic	HDF N=683	HD N=677
Age (years)	62,5±13 5	62,3±13, 5
History of CV disease (%)	43	47
Diabetes (%)	34	37
Dialysis vintage (median, mos)	35	30
Vascular access (%): Native fistula Catheter	 82 13	 82 14
Previous kidney transplantation (%)	14	12

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	High-Dose Hemodiafiltration (N=683)	High-Flux Hemodialysis (N=677)
Age — yr	62.5±13.5	62.3±13.5
Female sex — no. (%)	247 (36.2)	257 (38.0)
Region — no. (%)		
Western Europe	223 (32.7)	218 (32.2)
Eastern Europe	234 (34.3)	233 (34.4)
Southern Europe	226 (33.1)	226 (33.4)
Cardiovascular disease — no. (%)†		
Any	296 (43.3)	316 (46.7)
Coronary heart disease‡	130 (19.0)	147 (21.7)
Diabetes mellitus — no. (%)	230 (33.7)	251 (37.1)
Smoking — no./total no. (%)		
Never	360/683 (52.7)	318/673 (47.3)
Current	98/683 (14.3)	109/673 (16.2)
Past	225/683 (32.9)	246/673 (36.6)
Alcohol consumption — no./total no. (%)		
Never	357/679 (52.6)	343/674 (50.9)
Current	175/679 (25.8)	199/674 (29.5)
Past	147/679 (21.6)	132/674 (19.6)
Body-mass index — no. (%)§	27.4±5.6	27.5±5.7
Body-surface area — m²¶	1.86±0.22	1.86±0.22
Blood pressure before dialysis — mm Hg		
Systolic	141±22	141±22
Diastolic	73±14	72±15
Heart rate before dialysis — beats/min	72±11	72±12
Laboratory values		
Hemoglobin — g/dl	11.3±1.2	11.3±1.2
Serum creatinine — mg/dl‖	7.4±2.5	7.3±2.3
Serum urea — mg/dl	70.6±30.5	71.4±32.7
Median C-reactive protein (IQR) — mg/liter	5 (2–11)	4 (2–10)
Serum phosphate — mg/dl	4.9±1.5	4.9±1.4
Blood flow — ml/min**	369±54	367±56
Median residual urinary output (IQR) — ml/24 hr	850 (500–1300)	800 (444–1200)
Dialysis		
Median vintage (IQR) — mo	35 (16–78)	30 (14–67)
Median duration of session (IQR) — min	240 (240–248)	240 (240–245)
Median single-pool Kt/V (IQR)††	1.61 (1.45–1.83)	1.61 (1.42–1.80)
Vascular access — no. (%)		
Fistula	558 (81.7)	557 (82.3)
Catheter	90 (13.2)	94 (13.9)
Graft	35 (5.1)	26 (3.8)
Previous kidney transplantation — no. (%)	93 (13.6)	79 (11.7)

* Plus–minus values are means ±SD. Details regarding missing data (which were omitted from calculations of means and medians) are provided in Section S4 in the Supplementary Appendix. To convert the values for creatinine to micromoles per liter, multiply by 88.4. To convert the values for serum phosphate (as inorganic phosphorus) to millimoles per liter, multiply by 0.3229. IQR denotes interquartile range.

† Cardiovascular disease (including coronary heart disease) was defined as a history of any one or more of the following conditions: angina, myocardial infarction, coronary stent or dotter procedure and coronary-artery bypass graft, congestive heart failure, atrial fibrillation, transient ischemic attack, cerebrovascular accident, abdominal aortic aneurysm or intermittent claudication; placement of pacemaker or internal defibrillator; carotid endarterectomy; stent or

Results: outcome data

Table 2. Primary and Secondary Outcomes.*

Variable	High-Dose Hemodiafiltration (N=683)		High-Flux Hemodialysis (N=677)		Hazard Ratio (95% CI)†
	no. (%)	*no. of events/ 100 patient-yr (95% CI)*	*no. (%)*	*no. of events/ 100 patient-yr (95% CI)*	
Primary outcome					
Death from any cause	118 (17.3)	7.13 (5.90–8.54)	148 (21.9)	9.19 (7.77–10.79)	0.77 (0.65–0.93)
Secondary outcomes					
Death					
Cardiovascular	31 (4.5)	1.87 (1.27–2.66)	37 (5.5)	2.30 (1.62–3.17)	0.81 (0.49–1.33)
Noncardiovascular	87 (12.7)	5.26 (4.21–6.48)	111 (16.4)	6.89 (5.67–8.30)	0.76 (0.59–0.98)
Infection-related					
Including Covid-19	38 (5.6)	2.30 (1.62–3.15)	54 (8.0)	3.35 (2.52–4.37)	0.69 (0.49–0.96)
Excluding Covid-19	23 (3.4)	1.39 (0.88–2.09)	33 (4.9)	2.05 (1.41–2.88)	0.68 (0.42–1.10)
Fatal or nonfatal cardiovascular outcome‡	136 (19.9)	9.05 (7.60–10.71)	126 (18.6)	8.48 (7.07–10.10)	[illegible]
Kidney transplantation	75 (11.0)	4.80 (3.77–6.01)	71 (10.5)	4.72 (3.69–5.96)	1.01 (0.71–1.44)
Recurrent hospitalization — no.§					
For any nonfatal cause	998	61.34 (57.59–65.27)	895	56.36 (52.73–60.18)	1.11 (0.98–1.25)
Infection-related					
Including Covid-19	234	14.32 (12.54–16.28)	219	13.92 (12.14–15.88)	1.06 (0.86–1.30)
Excluding Covid-19	152	9.34 (7.92–10.95)	156	9.82 (8.34–11.49)	0.97 (0.74–1.26)

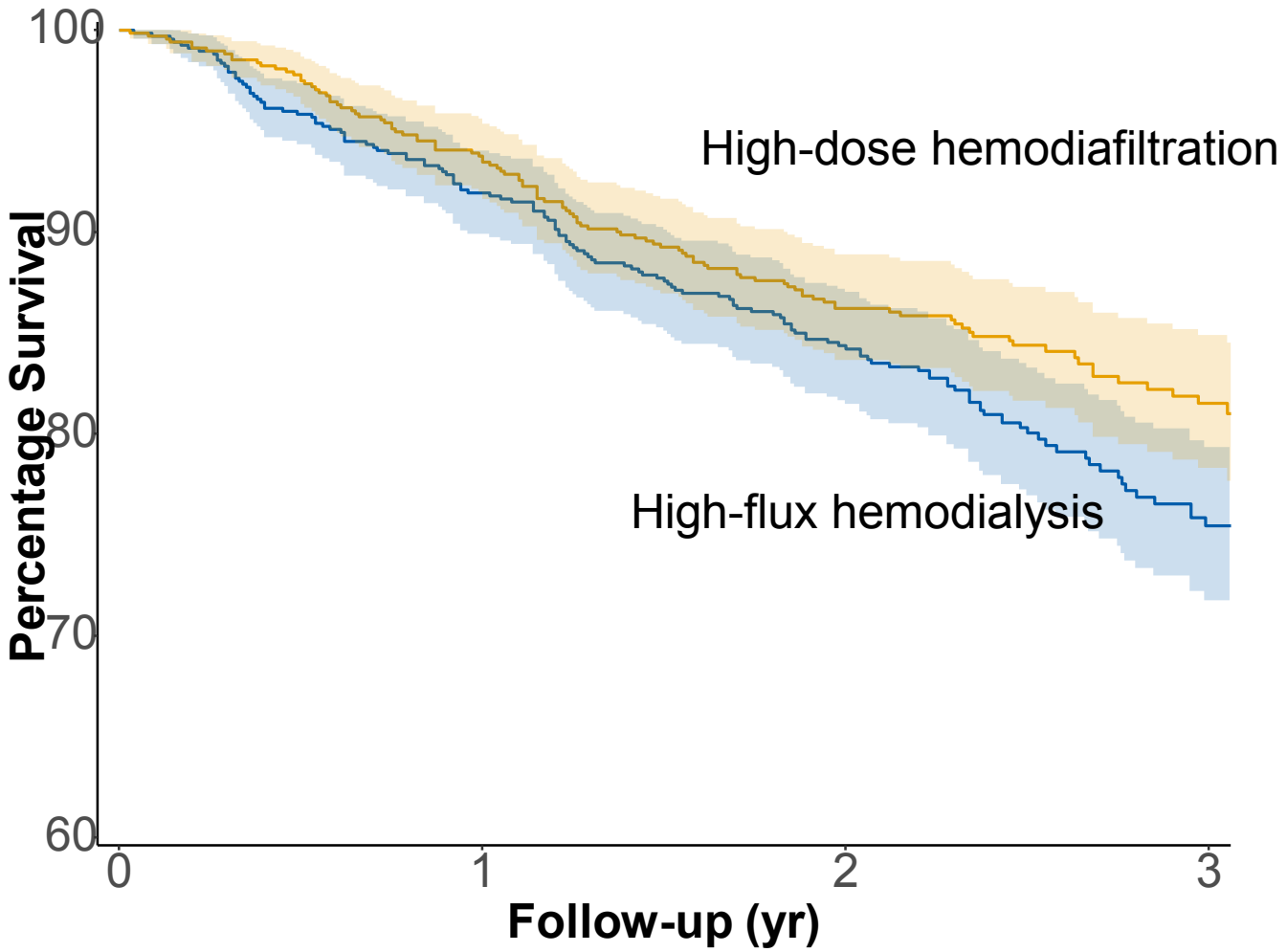
* All the listed analyses were prespecified except for the categories involving hospitalization or death from coronavirus disease 2019 (Covid-19).
† No adjustment for multiplicity was made, so the 95% confidence intervals should not be used in place of hypothesis testing.
‡ The composite outcome of fatal or nonfatal cardiovascular events includes death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, therapeutic coronary procedure (coronary-artery bypass grafting, percutaneous transluminal coronary angioplasty, or stenting), therapeutic carotid procedure (endarterectomy or stenting), vascular intervention (revascularization or percutaneous transluminal angioplasty or stenting), or peripheral limb amputation.
§ In this category, patients may have had more than one recurrent event, so percentages of patients are not provided.

→Comment ACM

→Comment CV death

→Comment infectious death

Kaplan Meier curves for overall survival

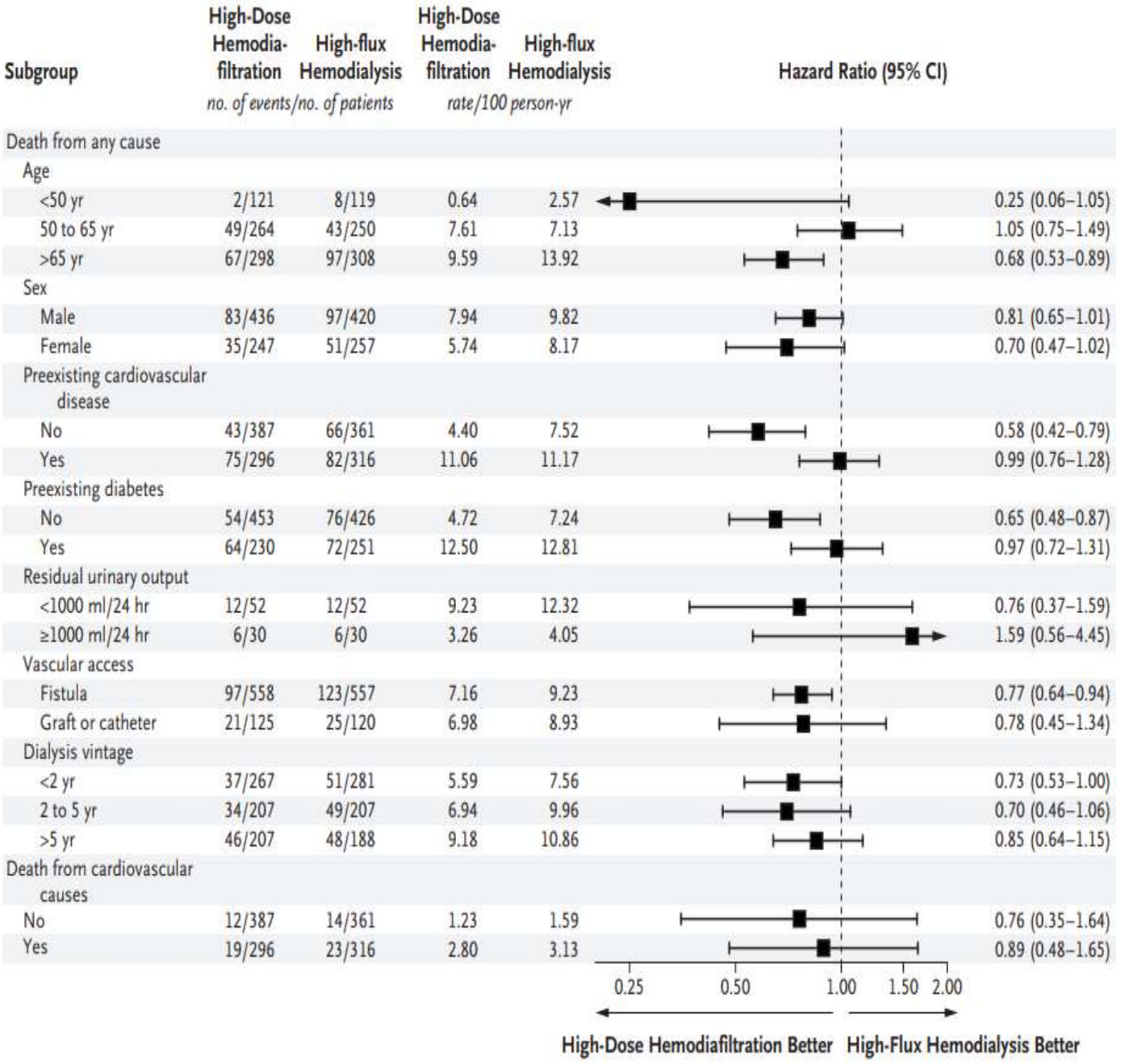


No. at Risk				
High-dose hemodiafiltration	683	625	519	194
High-flux hemodialysis	677	612	501	170
No. of Events				
High-dose hemodiafiltration	0	44	92	110
High-flux hemodialysis	0	54	105	140

→Comment age

→Comment DM

→Comment AVF



Subgroup	High-Dose Hemodia-filtration (no. of events/no. of patients)	High-flux Hemodialysis (no. of events/no. of patients)	High-Dose Hemodia-filtration (rate/100 person-yr)	High-flux Hemodialysis (rate/100 person-yr)	Hazard Ratio (95% CI)
Death from any cause					
Age					
<50 yr	2/121	8/119	0.64	2.57	0.25 (0.06–1.05)
50 to 65 yr	49/264	43/250	7.61	7.13	1.05 (0.75–1.49)
>65 yr	67/298	97/308	9.59	13.92	0.68 (0.53–0.89)
Sex					
Male	83/436	97/420	7.94	9.82	0.81 (0.65–1.01)
Female	35/247	51/257	5.74	8.17	0.70 (0.47–1.02)
Preexisting cardiovascular disease					
No	43/387	66/361	4.40	7.52	0.58 (0.42–0.79)
Yes	75/296	82/316	11.06	11.17	0.99 (0.76–1.28)
Preexisting diabetes					
No	54/453	76/426	4.72	7.24	0.65 (0.48–0.87)
Yes	64/230	72/251	12.50	12.81	0.97 (0.72–1.31)
Residual urinary output					
<1000 ml/24 hr	12/52	12/52	9.23	12.32	0.76 (0.37–1.59)
≥1000 ml/24 hr	6/30	6/30	3.26	4.05	1.59 (0.56–4.45)
Vascular access					
Fistula	97/558	123/557	7.16	9.23	0.77 (0.64–0.94)
Graft or catheter	21/125	25/120	6.98	8.93	0.78 (0.45–1.34)
Dialysis vintage					
<2 yr	37/267	51/281	5.59	7.56	0.73 (0.53–1.00)
2 to 5 yr	34/207	49/207	6.94	9.96	0.70 (0.46–1.06)
>5 yr	46/207	48/188	9.18	10.86	0.85 (0.64–1.15)
Death from cardiovascular causes					
No	12/387	14/361	1.23	1.59	0.76 (0.35–1.64)
Yes	19/296	23/316	2.80	3.13	0.89 (0.48–1.65)

RESEARCH SUMMARY

Effect of Hemodiafiltration or Hemodialysis on Mortality in Kidney Failure

Blankestijn PJ et al. DOI: 10.1056/NEJMoa2304820

CLINICAL PROBLEM

Hemodiafiltration and hemodialysis are two methods of treating kidney failure. Data comparing survival outcomes with these approaches have been largely inconclusive; results of one randomized, controlled trial indicating a lower risk of death with hemodiafiltration may have reflected confounding bias.

CLINICAL TRIAL

Design: A multinational, pragmatic, open-label, randomized, controlled trial assessed the benefits and harms of high-dose hemodiafiltration as compared with conventional high-flux hemodialysis in patients with kidney failure.

Intervention: 1360 adults with stage V kidney failure who had received hemodialysis for ≥3 months were assigned to receive high-dose hemodiafiltration (a convection volume of ≥23 liters in postdilution mode per session) or continuation of high-flux hemodialysis. The primary outcome was death from any cause.

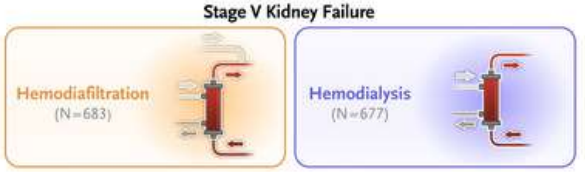
RESULTS

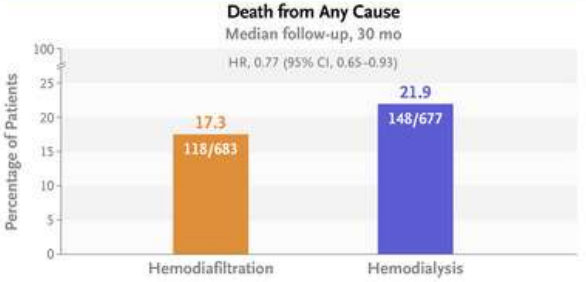
Outcomes: During a median follow-up of 30 months, the risk of death from any cause was lower in patients receiving high-dose hemodiafiltration than in those receiving hemodialysis. The survival effect of hemodiafiltration appeared to be limited to those without a history of cardiovascular disease or diabetes.

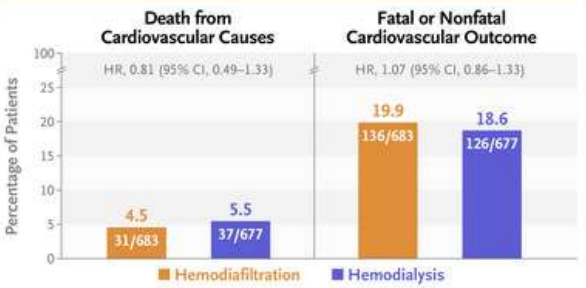
LIMITATIONS AND REMAINING QUESTIONS

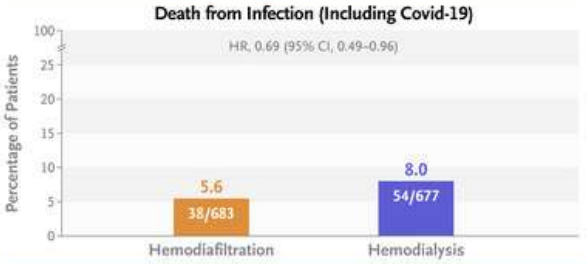
- The achieved sample size was lower than originally planned because of difficulty recruiting patients during the Covid-19 pandemic.
- Inclusion criteria may have resulted in a trial population that was healthier than the general population of patients who receive hemodialysis in Europe and the United States.
- Findings may not be generalizable beyond White European populations.

Links: Full Article | NEJM Quick Take | Editorial









CONCLUSIONS

In adults with kidney failure, the risk of death from any cause was lower in patients receiving high-dose hemodiafiltration than in those receiving high-flux hemodialysis.

DOBBIAMO PERSONALIZZARE IL TRATTAMENTO DIALITICO!!!

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**.

Chapdelaine I, 2015

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.

Chapdelaine I, 2015


Paramount+