# Διευρυμένη Αιμοκάθαρση (Expanded Hemodialysis)

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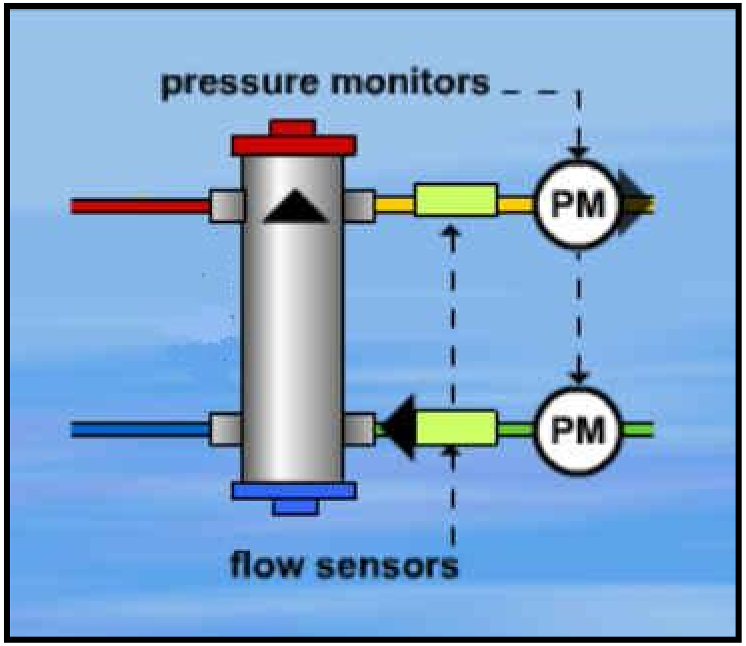
# ΑΙΜΟΚΑΘΑΡΣΗ

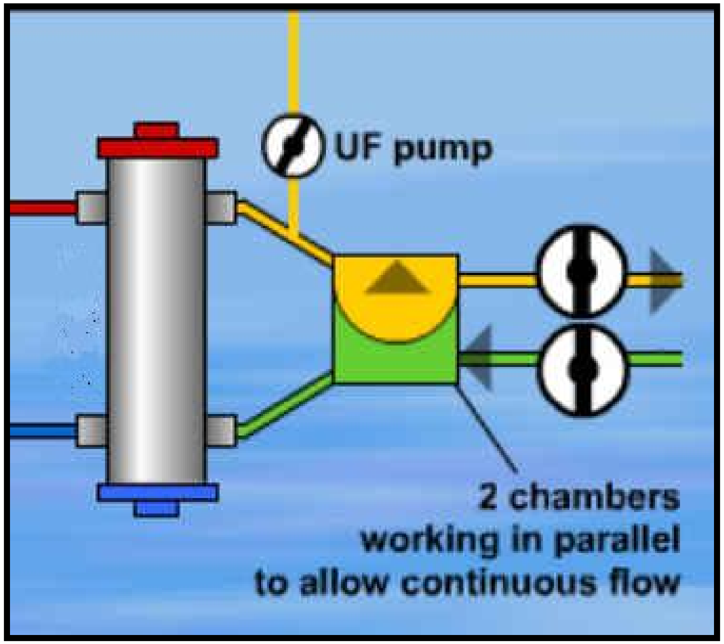
Μέθοδος υποκατάστασης της νεφρικής λειτουργίας κατα την οποία πραγματοποιείται διΰλιση του αίματος μέσω ημιδιαπερατής μεμβράνης και επιτυγχάνεται:

- Αφαίρεση υγρών
- Κάθαρση «άχρηστων» ουσιών

# Σύγχρονα συστήματα ελέγχου υπερδιήθησης

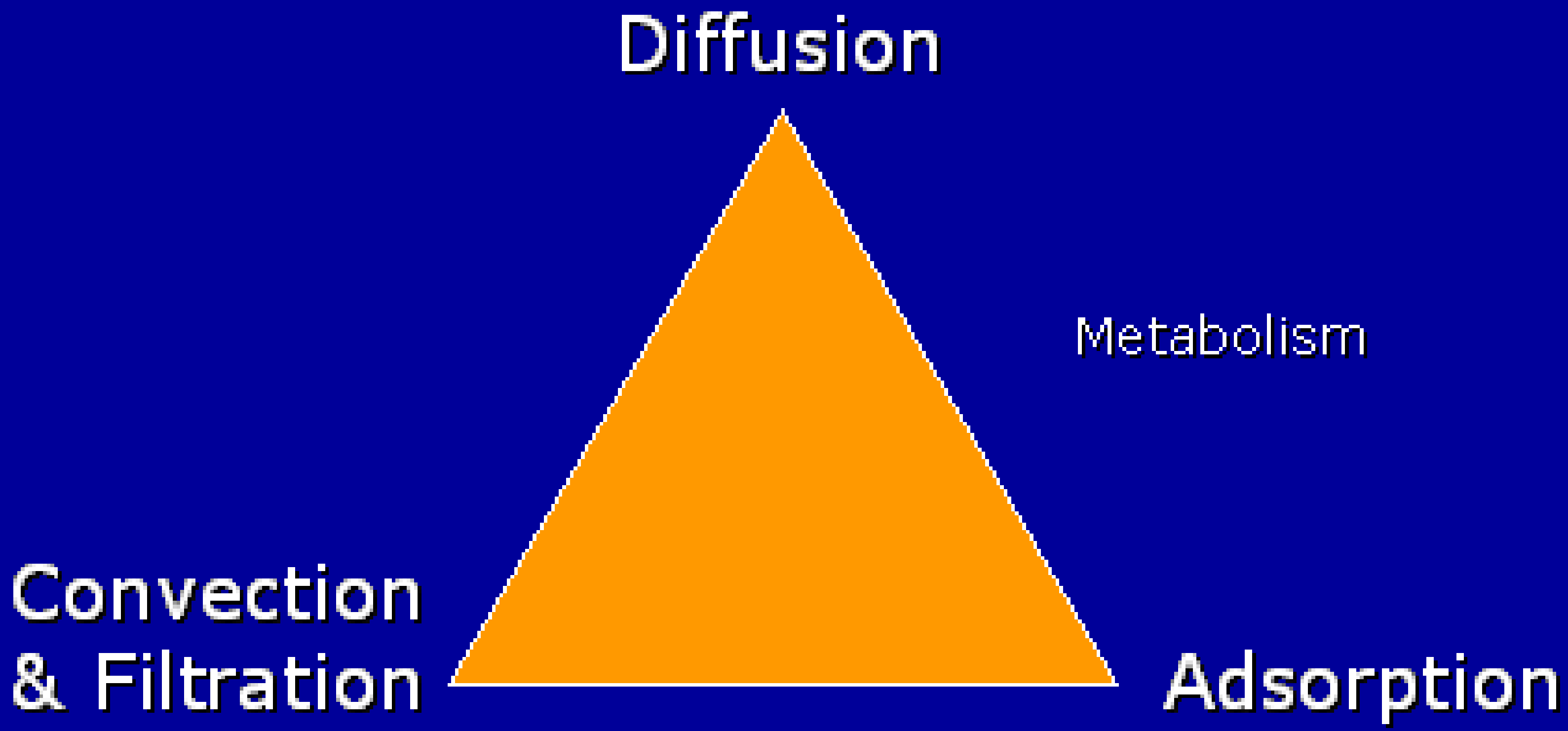



Open (Sensor) System




Closed (Balance Chamber) System

# Extracorporeal Solute Removal



# Χαρακτηριστικά Μεμβρανών

1. Υλικό
2. Επιφάνεια
3. Αποστείρωση
4. Όγκος πλήρωσης
5. Πάχος μεμβράνης
6. Κάθαρση ουσιών α) μικρού Μ.Β. (ουρία, κρεατινίνη, φωσφορικά) β) μέσου Μ.Β. (Β12, β2-μικροσφαιρίνη)
7. Συντελεστής διαβατότητας της μεμβράνης για συγκεκριμένη ουσία (Sieving Coefficient – Sc)-εξαρτάται απο τους **πόρους της μεμβράνης**

Για ουσίες μικρού Μ.Β. είναι ίσος προς την μονάδα άσχετα από το είδος της μεμβράνης

8. Συντελεστής υπερδιήθησης (Ultrafiltration Coefficient – UF.C. σε ml/h/mmHg)

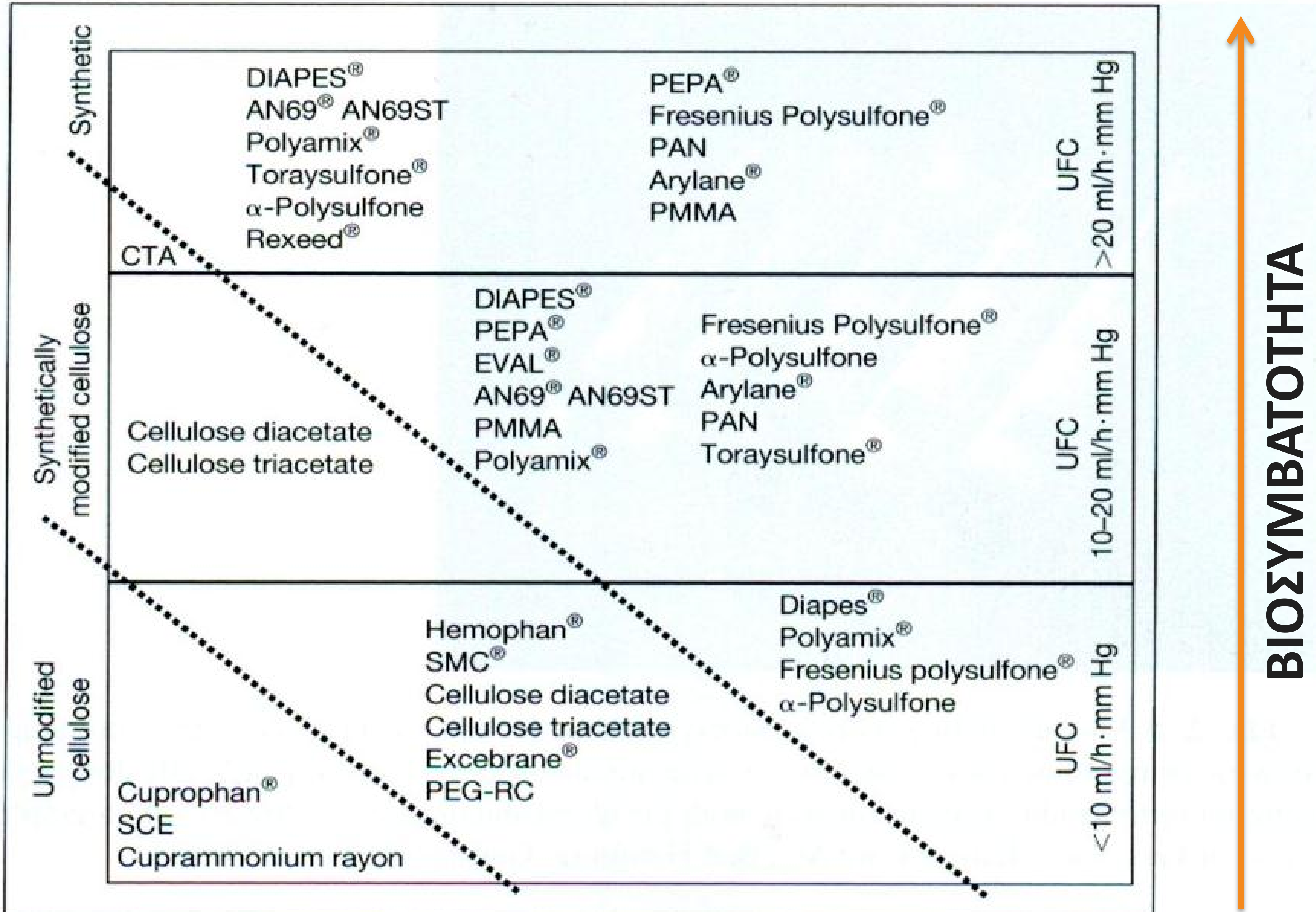
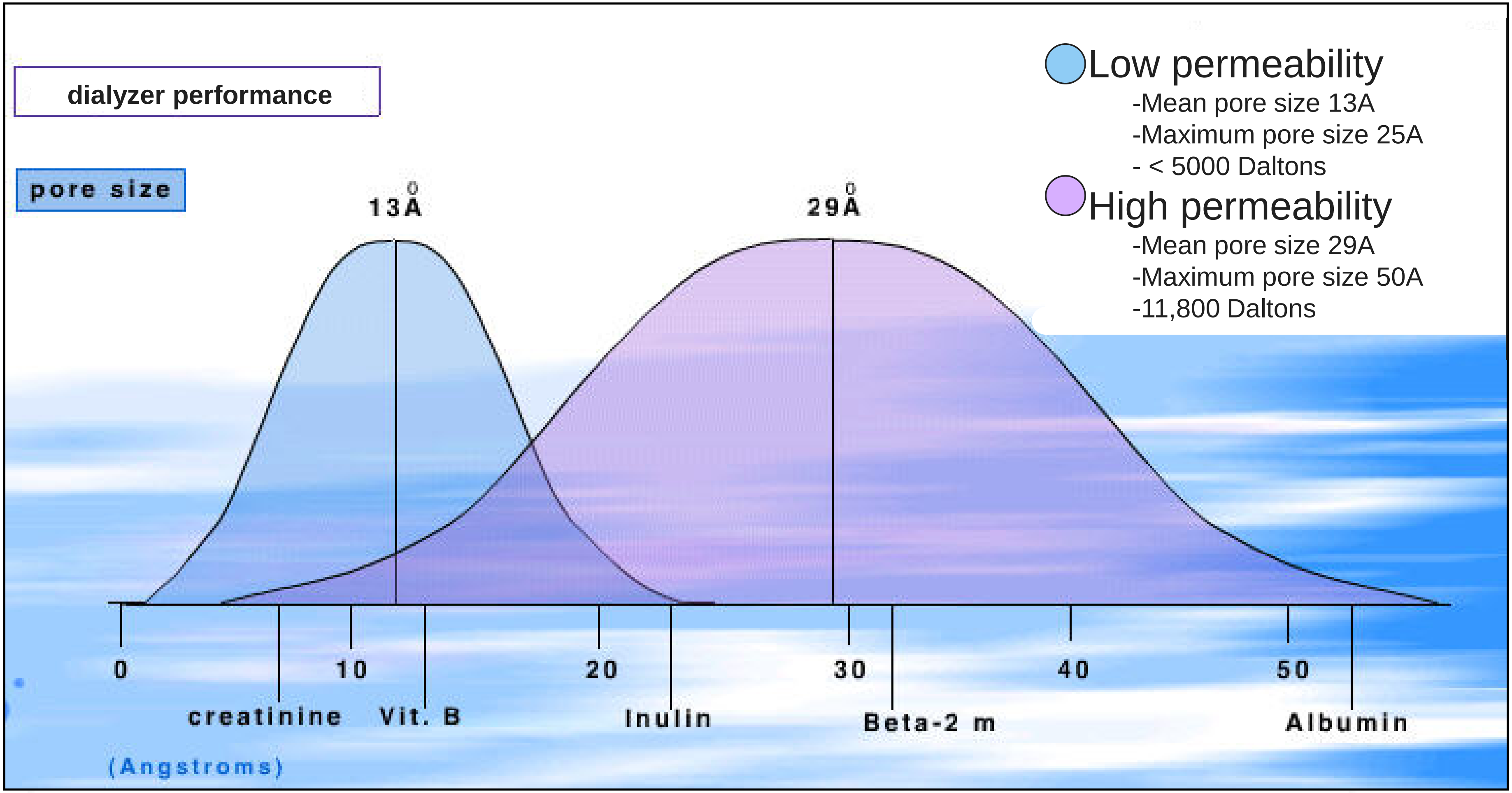



***Fig. 1.*** Membranes suitable for haemodiafiltration classified according to their chemical composition and hydraulic permeability. UFC = Ultrafiltration coefficient.

# Διαπερατότητα της Μεμβρανης

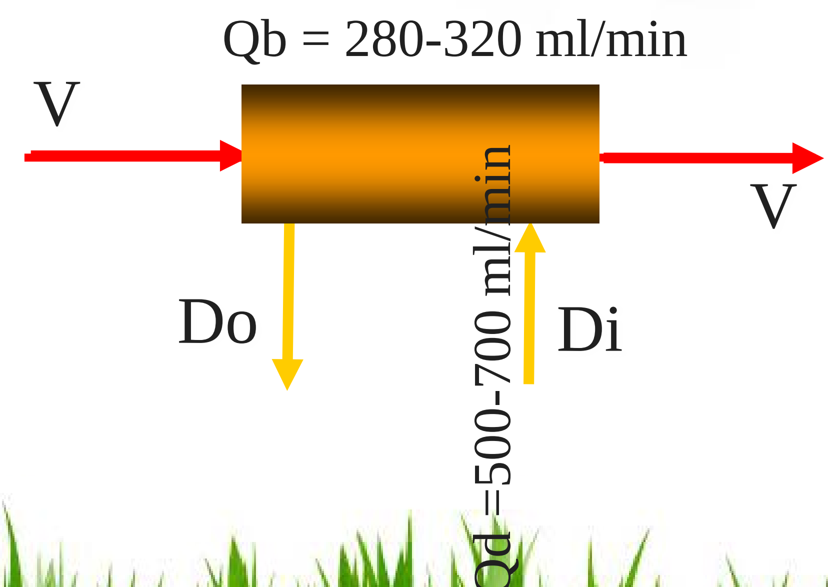


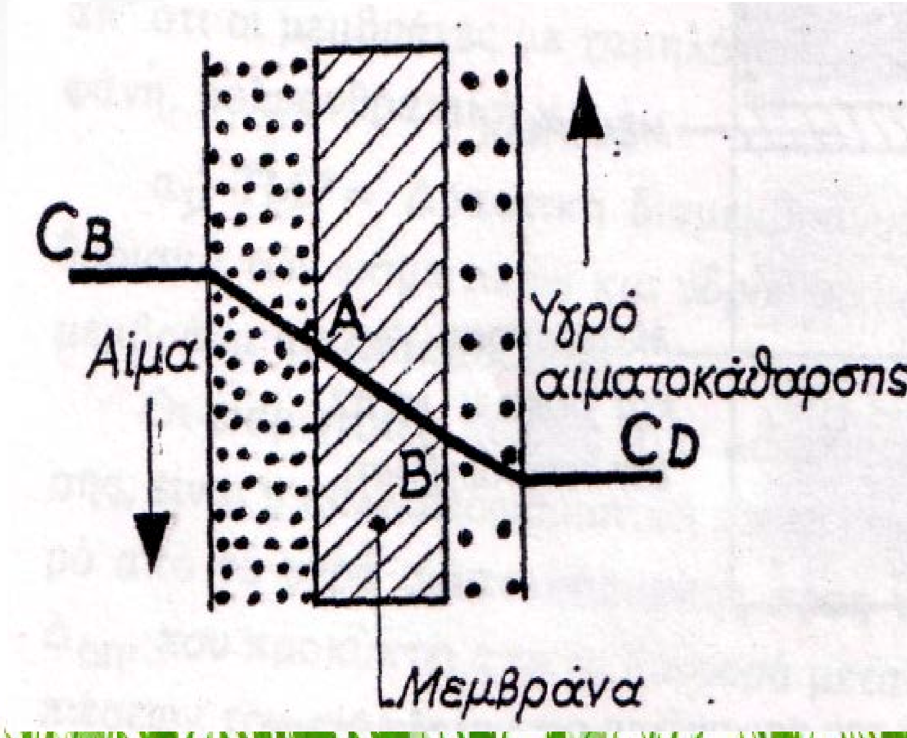
# ΤΕΧΝΙΚΕΣ ΑΙΜΟΚΑΘΑΡΣΗΣ

- **Low flux AMK**
- **High flux AMK**
- **Αιμοδιαδιήθηση**

# Low flux Αιμοκάθαρση

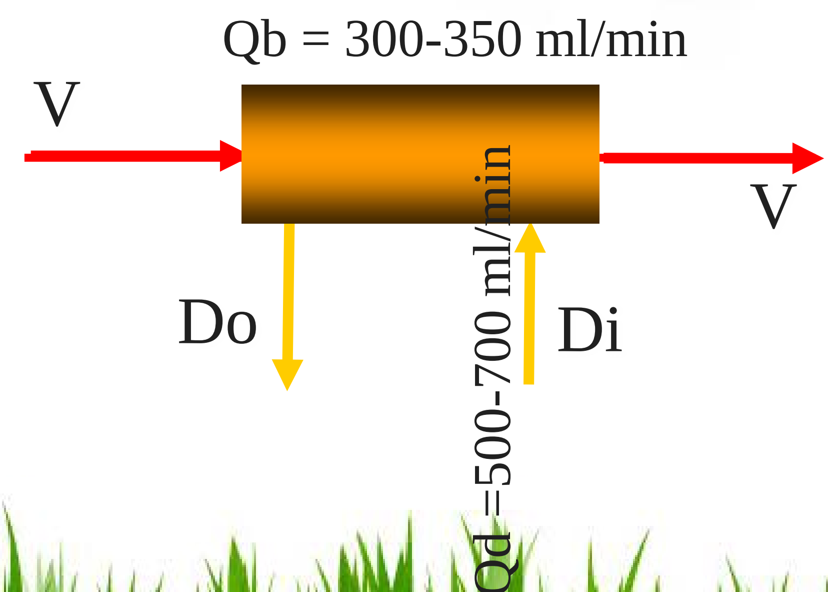
- Κλασσική ΑΜΚ με φίλτρα χαμηλής διαπερατότητας (διάχυση)
- Χαμηλού κόστους
- Η φθηνότερη θεραπεία που υπάρχει σήμερα

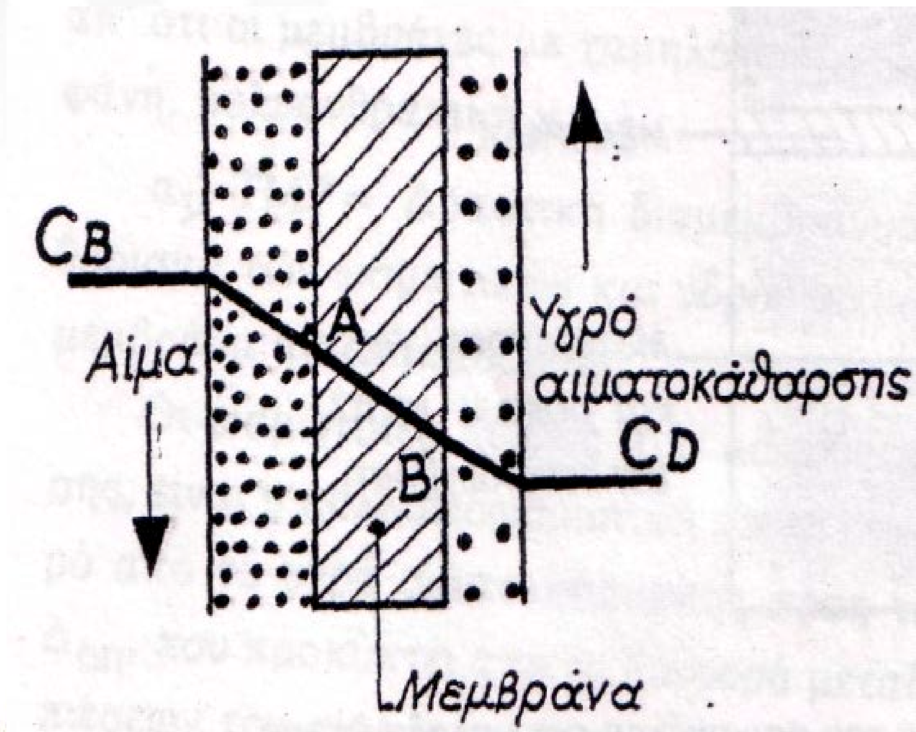


# High flux Αιμοκάθαρση

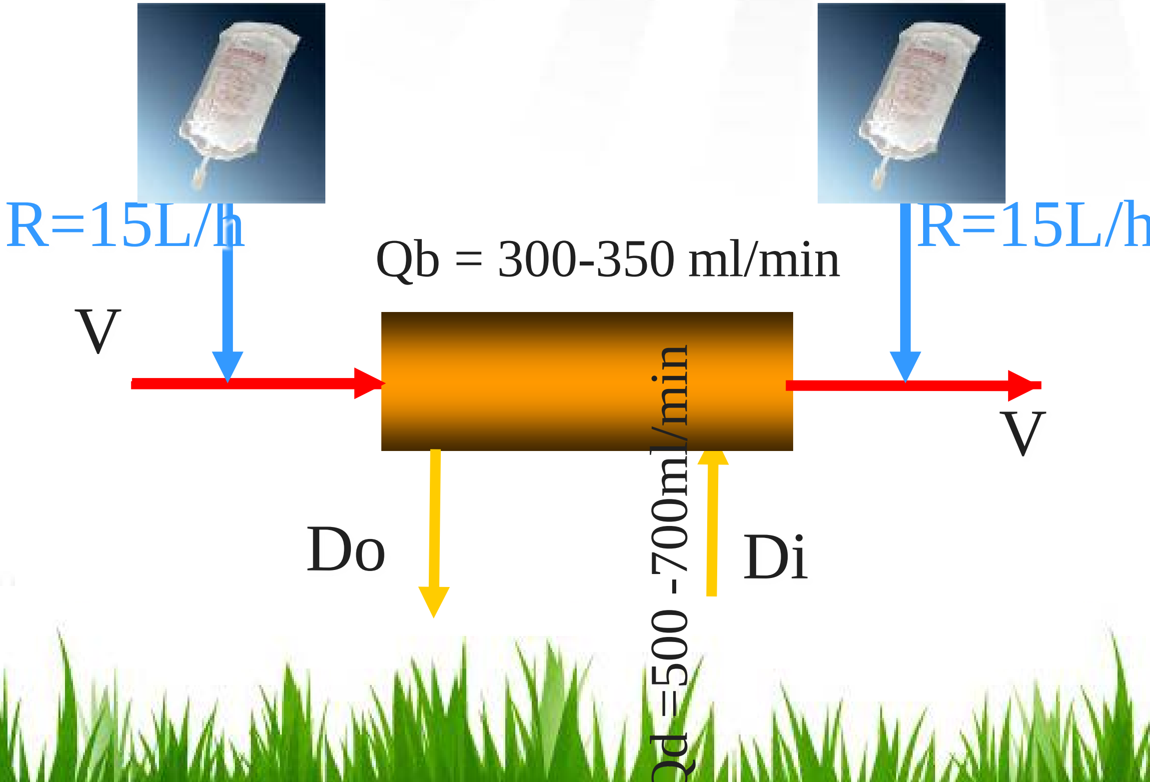
- Κλασσική ΑΜΚ με φίλτρα υψηλής διαπερατότητας (διάχυση)
- Υψηλότερου κόστους
- Καλύτερη κάθαρση (ΜΜΒ ουσιών)



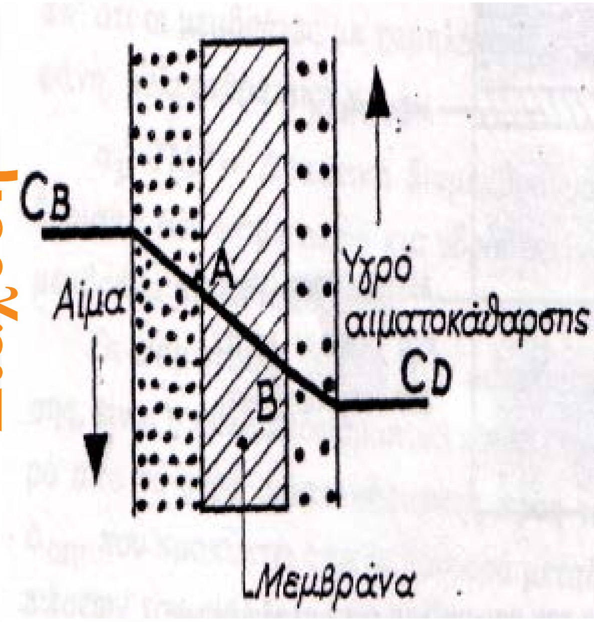



# Αιμοδιαδίηθηση

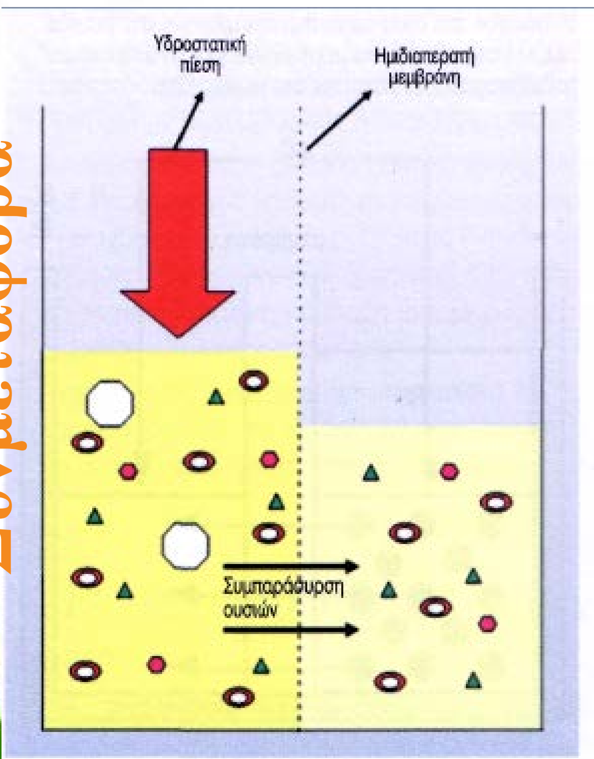
- Παραλλαγή της ΑΜΚ με φίλτρα υψηλής διαπερατότητας
- Χρησιμοποιεί την διάχυση και την «συνμεταφορά»
- Αρχικά σάκοι αιμοδίηθησης
- Υψηλότερο κόστος
- Πολύ καλύτερη κάθαρση (ΜΜΒ ουσιών)




Διάχυση

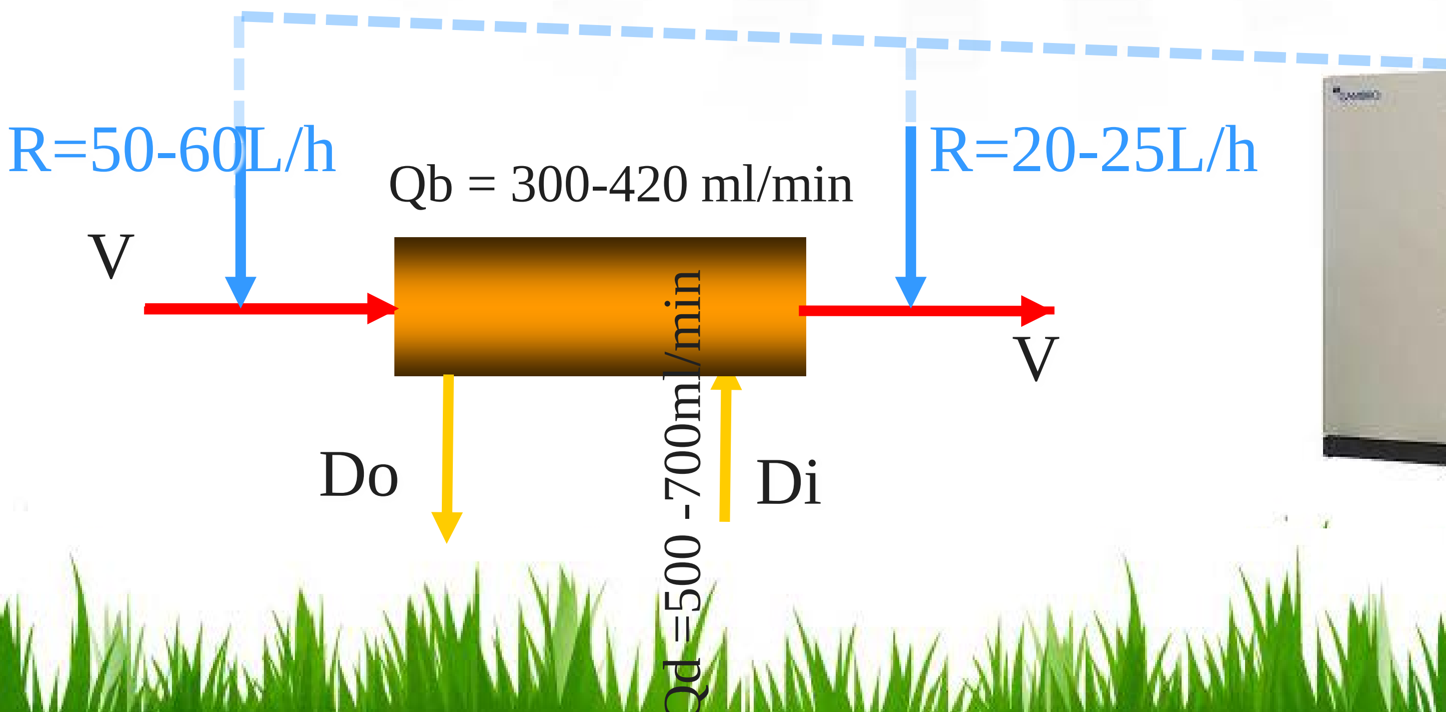



Συμμεταφορά

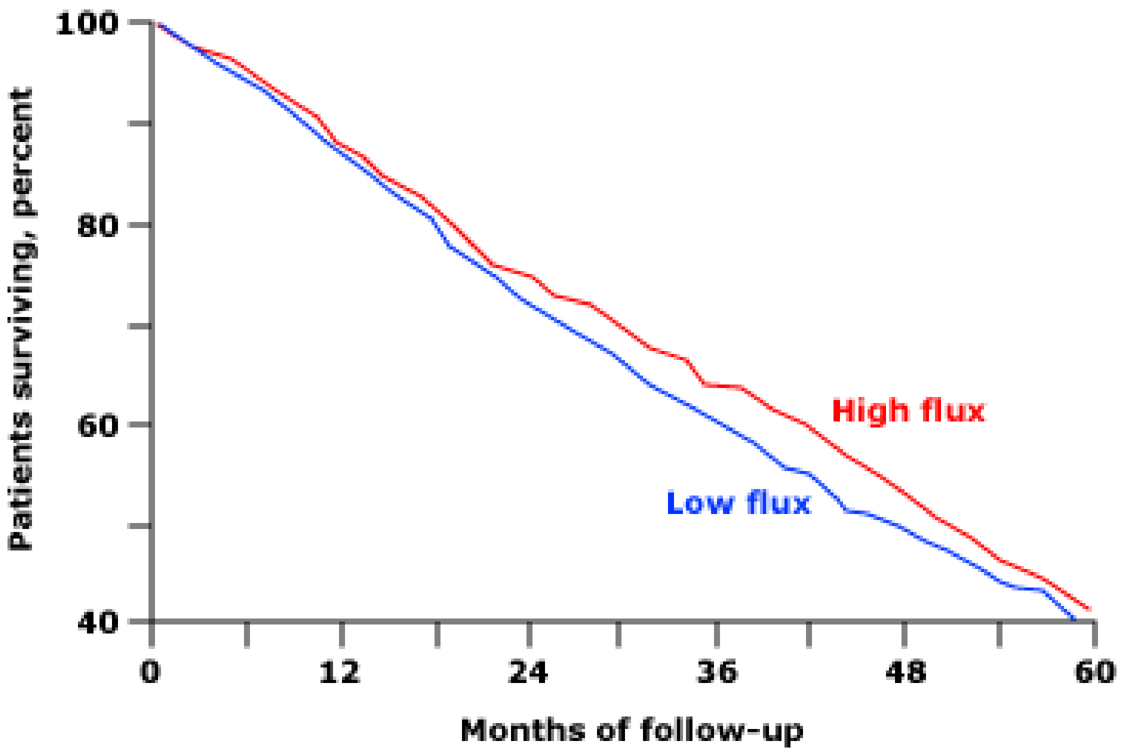


# On line Αιμοδιαδιήθηση

- Βελτίωση της αιμοδιαδιήθησης
- Χρησιμοποιεί την διάχυση και την «συνμεταφορά»
- Απαιτεί υψηλής ποιότητος επεξεργασμένο νερό
- Εξειδικευμένα μηχανήματα
- Ειδικές γραμμές(φιλτράκια)-Υψηλές αντλίες αίματος
- Ακόμα υψηλότερο κόστος
- Ακόμα καλύτερη κάθαρση (ΜΜΒ ουσιών)

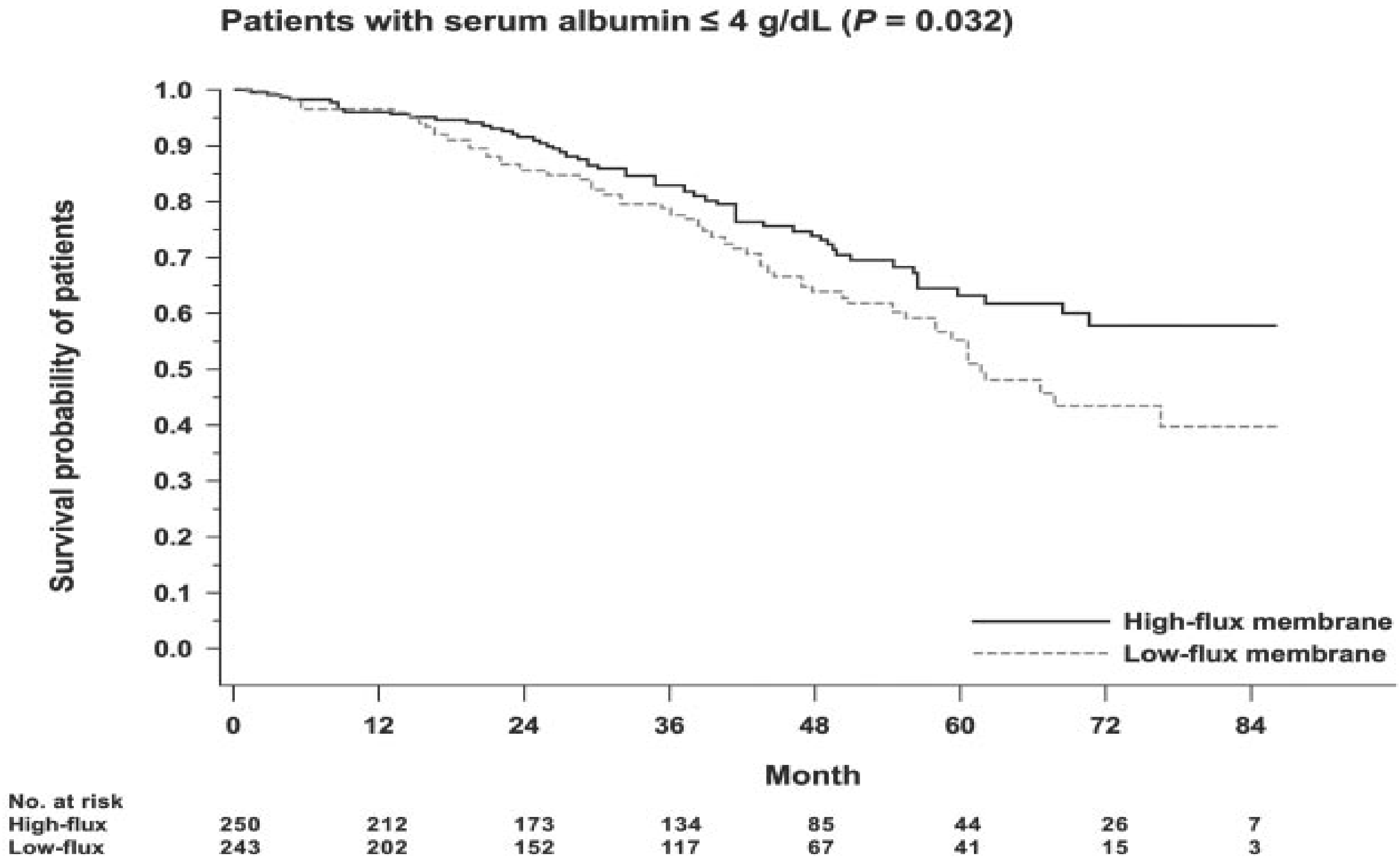



# Μελέτες επιβίωσης – HEMO study



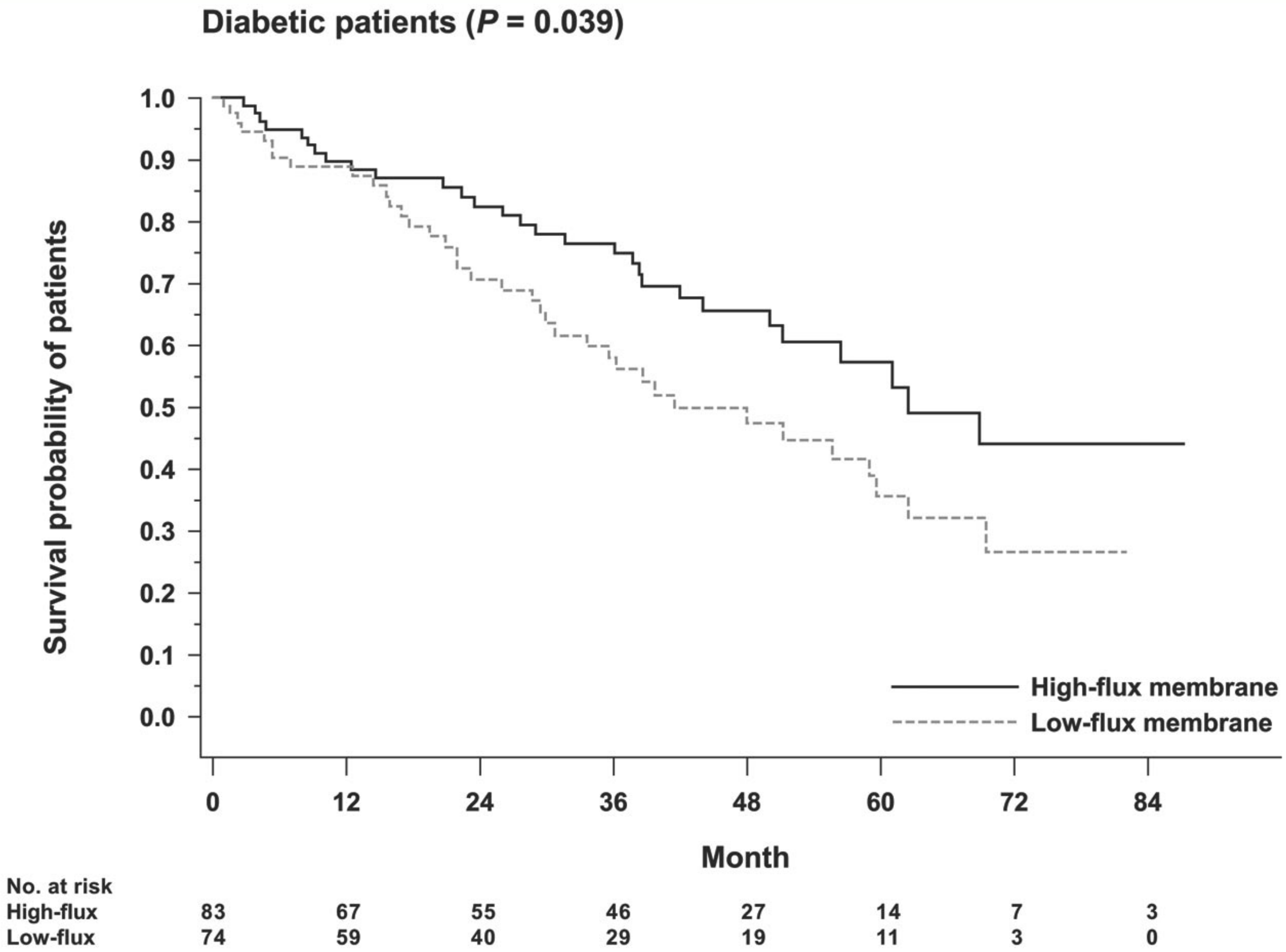

Eknoyan G et al.Effect of dialysis dose and membrane flux in maintenance Hemodialysis. N Engl J Med 2002;347:2010

# Μελέτες επιβίωσης-ΜΡΟ




Locatelli F et al. Effect of membrane permeability on survival of Hemodialysis patients. J Am Soc Nephrol **20:** 645–654, 2009

# Μελέτες επιβίωσης-MPO

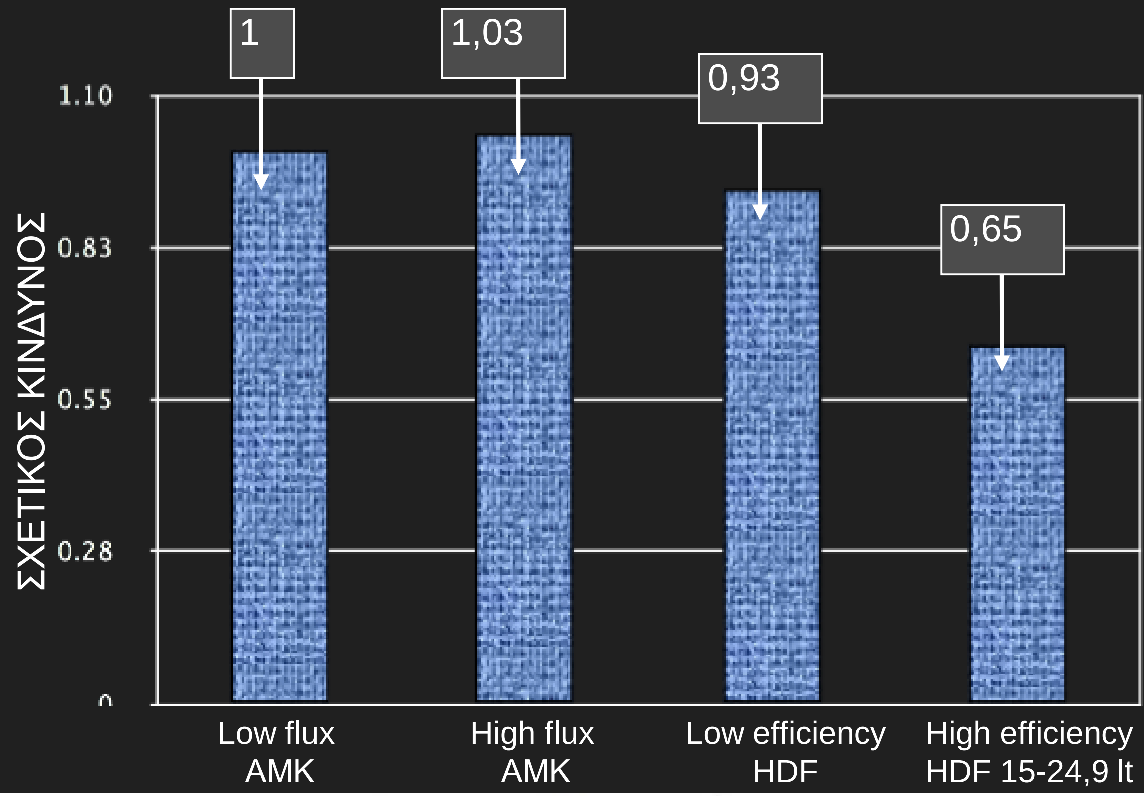



Locatelli F et al. Effect of membrane permeability on survival of Hemodialysis patients. J Am Soc Nephrol **20:** 645–654, 2009

# Μελέτες επιβίωσης
# DOPPS study

Mortality risk for patients receiving hemodiafiltration vs hemodialysis:European results from the DOPPS.
B.Canaud et al. Kidney International 2006 (69) 2087-2093.

Ο σχετικός κίνδυνος για τη θνητότητα, φαίνεται να είναι σαφώς μικρότερος για τους ασθενείς που υποβάλλονται σε Αιμοδιαδιήθηση, ιδιαίτερα όταν χρησιμοποιούνται υψηλοί όγκοι διαλύματος (high efficiency HDF)



# A role of large middle molecules is supported by the outcome benefit of HDF seen in RCTs

Pooled data analysis of mortality using four RCTs comparing post-dilution HDF to HD

| Mortality Cause | HD | HDF | Hazard Ratio (95%CI) for HDF vs HD | |
|---|---|---|---|---|
| | Events/ 100PY | Events/ 100PY | | |
| **All-cause** | **12.1** | **10.4** | **0.86 (0.75;0.99)** | **Greater effect in older patients, age >65y** [p=0.03 for CV mortality] |
| **Cardiovascular disease** | **4.8** | **3.7** | **0.77 (0.61;0.97)** | |
| **Infections** | **2.3** | **2.1** | **No significant difference** | |
| **Sudden death** | **1.6** | **1.6** | **No significant difference** | |

Including data from CONTRAST, Turkish HDF, ESHOL, and French HDF studies
CI = confidence intervall; PY = person-years

*Peters et al., Nephrol Dial Transplant 2016;31:978-84*

Nephrol Dial Transplant (2007) 22 [Suppl 2]: ii5–ii21
doi:10.1093/ndt/gfm022

NDT
Nephrology Dialysis Transplantation

EBPG guideline on dialysis strategies

# 2. Flux and convection

## Guideline 2.1

**The use of synthetic high-flux membranes should be considered to delay long-term complications of haemodialysis therapy. Specific indications include;**

**(i) To reduce dialysis-related amyloidosis (III)**
**(ii) To improve control of hyperphosphataemia (II)**
**(iii) To reduce the increased cardiovascular risk (II)**
**(iv) To improve control of anaemia (III)**

## Guideline 2.2

**In order to exploit the high permeability of high-flux membranes, on-line haemodiafiltration or haemofiltration should be considered.**

**The exchange volumes should be as high as possible, with consideration of safety. (Evidence level II).**

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EBPG guideline on dialysis strategies -2010 revised

# The existing Guideline 2.1 should thus be replaced by the following:

- Synthetic high-flux membranes should be used to delay long-term complications of haemodialysis therapy in patients at high risk (serum albumin <40 g/l) (level 1A: strong recommendation, based on high-quality evidence).
- In view of underlying practical considerations, and the observation of a reduction of an intermediate marker (beta-2-microglobulin), synthetic high-flux membranes should be recommended even in low-risk patients (level 2B: weak recommendation, low quality evidence).

# Μελέτες υπεροχής on line αιμοδιαδιήθησης καλύτερη κάθαρση ουσιών μέσου Μ.Β.

| | Μείωση β2 μικροσφαιρίνης/συνεδρία |
|---|---|
| Low flux αιμοκάθαρση | 20% |
| High flux αιμοκάθαρση | 60% |
| On line αιμοδιαδιήθηση | 75% |

Maduell F et al. Osteocalcin and myoglobin removal in on-line hemodiafiltration versus low- and high-flux hemodialysis. Am J Kidney Dis 2002;40(3):582

# Οι σημερινές τεχνικές Αιμοκάθαρσης έχουν περιορισμούς στην κάθαρση ουραιμικών τοξινών μεγάλου MB

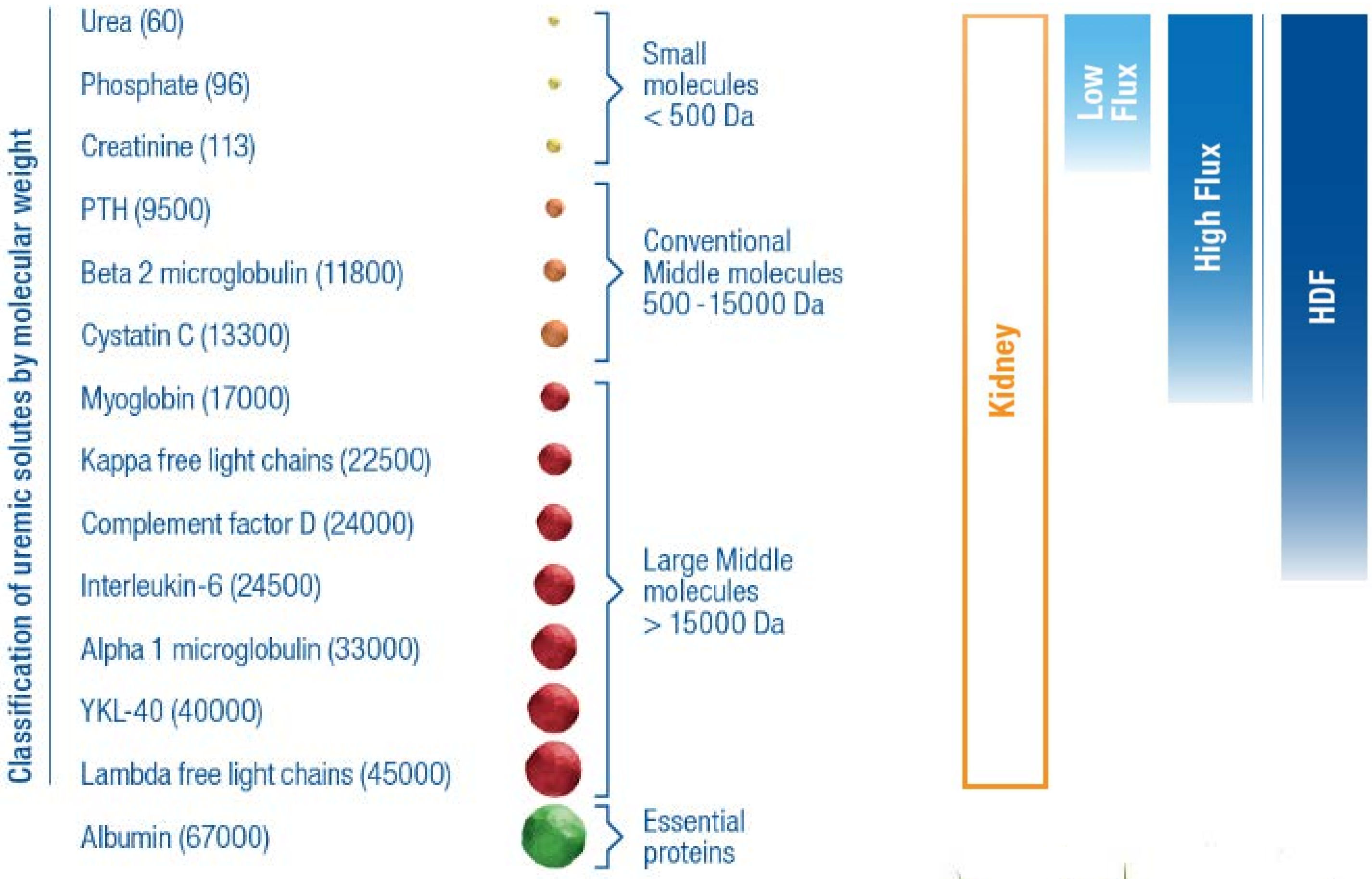


**Table 1. Summary of middle molecules (*n*=59)**

| Removed by High Flux (<15 kD) | Molecular Mass, kD | Removed by HDF (15–24.9 kD) | Molecular Mass, kD | Not Currently Removed (>25 kD) | Molecular Mass, kD |
|---|---|---|---|---|---|
| Methionine-enkephalin | 0.5 | Clara cell protein | 15.8 | Hyaluronic acid | 25 |
| Glutathione | 0.6 | Leptin | 16 | $\beta$-Trace protein | 26 |
| Angiotensin A | 0.8 | Myoglobin | 17 | Soluble TNF receptor-1 | 27 |
| $\delta$–Sleep-inducing peptide | 0.8 | TNF-$\alpha$ | 17 | Adiponectin | 30 |
| Dinucleoside polyphosphates | 1 | Soluble TNF receptor-2 | 17 | FGF-23 | 32 |
| Substance P | 1.3 | IL-1$\beta$ | 17.5 | $\alpha$1-Microglobulin | 33 |
| Motilin | 2.7 | FGF-2 | 18 | VEGF | 34.2 |
| Orexin B | 2.9 | IL-10 | 18 | YKL-40 | 40 |
| Atrial natriuretic peptide | 3 | Retinol binding protein | 21.2 | Pentraxin-3 | 40.2 |
| Desacylgherlin | 3.2 | Prolactin | 22 | $\alpha$1-Acid glycoprotein | 43 |
| Vasoactive interstinal peptide | 3.3 | $\kappa$-Ig light chain | 22.5 | AGEs | 45 |
| Calcitonin | 3.4 | Complement factor D | 23.75 | $\lambda$-Ig light chain | 45 |
| Gherlin | 3.4 | IL-18 | 24 | Visfatin | 55 |
| $\beta$-Endorphin | 3.4 | IL-6 | 24.5 | AOPPs | >60 |
| Orexin A | 3.5 | | | | |
| Calcitonin gene–related peptide | 3.7 | | | | |
| Cholecystokinin | 3.8 | | | | |
| Endothelin | 4.2 | | | | |
| Neuropeptide Y | 4.2 | | | | |
| SIAM-1 | 4.2 | | | | |
| Adrenomedullin | 5.7 | | | | |
| Osteocalcin | 5.8 | | | | |
| IGF-1 | 7.6 | | | | |
| IL-8 | 8 | | | | |
| Parathyroid hormone | 9.5 | | | | |
| Guanylin | 10.3 | | | | |
| $\beta$2-Microglobulin | 11.8 | | | | |
| Uroguanylin | 12 | | | | |
| Resistin | 12.5 | | | | |
| Cystatin C | 13.3 | | | | |
| Degranulation inhibiting protein[a] | 14.1 | | | | |

Thirty-one molecules had molecular mass under 15 kD, and therefore, they can be removed by high-flux dialysis. Fourteen molecules had molecular mass between 15 and 25 kD, and therefore, they can be removed by HDF. Fourteen molecules had molecular mass >25 kD. HDF, hemodiafiltration; FGF, fibroblast growth factor; VEGF, vascular endothelial growth factor; AGE, advanced glycosylation end product; AOPP, advanced oxidative protein products.
[a]Degranulation inhibiting protein corresponds to angiogenin.

Wolley et al. Large Middle Molecules and Hemodialysis. Clin J Am Soc Nephrol 13, May, 2018

**Table 1.** Uremia retention solutes inadequately cleared by current hemodialysis techniques [42]

| Solute | MW, Da | | Action/effect |
|---|---|---|---|
| β-2M | 12,000 | | Amyloidosis CTS |
| Leptin | 16,000 | Middle* | Malnutrition |
| Myoglobin | 17,000 | | Organ damage |
| κ-FLC | 23,000 | | Toxicity |
| Prolactin | 23,000 | | Infertility |
| Interleukin-6 | 25,000 | Large* | Inflammation |
| Hepcidin | 27,000 | | Anemia |
| Bound p-cresol | 33,500 | | CV toxicity |
| Pentraxin-3 | 43,000 | | Acute phase protein |
| λ-FLC | 45,000 | | CV toxicity |
| TNF-α (trim) | 51,000 | | Inflammation |

* Value referred to as the molecular weight interval between urea and albumin. β-2M, β2-microglobulin; κ-FLC, kappa free light chains; λ-FLC, lambda free light chains.

Ronco C (ed): Expanded Hemodialysis – Innovative Clinical Approach in Dialysis. Contrib Nephrol. Basel, Karger, 2017, vol 191, pp 188–199

**Table 3. Involvement of large middle molecules with cardiovascular disease**

| Middle Molecule | Association | Possible Mechanisms |
|---|---|---|
| IL-18 | Cardiovascular mortality; aortic pulse wave velocity; unstable coronary plaque; coronary and thoracic aortic calcification | Promotion of atherosclerotic plaque instability, induction of IFN-$\gamma$, promotion of collagen and lipid deposition |
| IL-6 | Left ventricular hypertrophy, systolic dysfunction; cardiovascular mortality | Coordination of local inflammatory cell influx and lymphocyte proliferation; promotion of coagulation |
| IL-1$\beta$ | Left ventricular hypertrophy | Promotion of local inflammatory response within plaque |
| TNF-$\alpha$ | Left ventricular hypertrophy | Promotion of cardiac inflammatory response to stress |
| Pentraxin-3 | Unstable coronary plaque | Infiltration of neutrophils into atherosclerotic plaque, prothrombotic effects, impairment of NO production |
| $\beta$-Trace protein | Atherosclerotic plaque; cardiovascular mortality | Possible functions acting against platelet aggregation *via* catalyzation of PGD2 production |
| Prolactin | Cardiovascular mortality | Proliferation of vascular smooth muscle cells, promotion of vasoconstriction |
| AGEs | Cardiovascular mortality | Deposition within vessel wall; induction of oxidative stress, inflammation, and endothelial dysfunction |
| Visfatin | Unstable atherosclerotic plaque | Induction of inflammatory macrophages within atherosclerotic plaque |
| Adiponectin | Atherosclerotic plaque | Expression of adhesion molecules; foam cell formation |
| Leptin | Atherosclerotic plaque | Expression of adhesion molecules; production of MCP-1, IL-6, and TNF-$\alpha$ |
| FGF-2 | Cardiac hypertrophy | Induction of cardiomyocyte hypertrophic response |
| FGF-23 | Cardiac hypertrophy | Induction of cardiomyocyte hypertrophic response |

NO, nitric oxide; AGE, advanced glycosylation end products FGF, fibroblast growth factor.

Wolley et al. Large Middle Molecules and Hemodialysis. Clin J Am Soc Nephrol 13, May, 2018

# Μέσου Μοριακού Βάρους ουσίες και Ανοσοποιητικό

**Table 4. Involvement of large middle molecules with secondary immunodeficiency**

| Middle Molecule | Associations | Possible Mechanisms |
|---|---|---|
| Ig light chains | Impaired PMNL function; infectious mortality | Interference with caspase-3 activity; interference with normal PMNL apoptosis |
| Retinol binding protein 4 | Impaired PMNL function | Interference with upstream complement receptor signaling within PMNLs |
| FGF-23 | Leukocyte inhibition | Interference with chemokine signaling |
| $\alpha$1-Acid glycoprotein | Impaired PMNL function | Neutrophil migration |

PMNL, polymorphonuclear leukocyte; FGF, fibroblast growth factor.

Wolley et al. Large Middle Molecules and Hemodialysis. Clin J Am Soc Nephrol 13, May, 2018

Editorial

Blood Purification

Blood Purif 2017;44:I–VIII
DOI: 10.1159/000476012

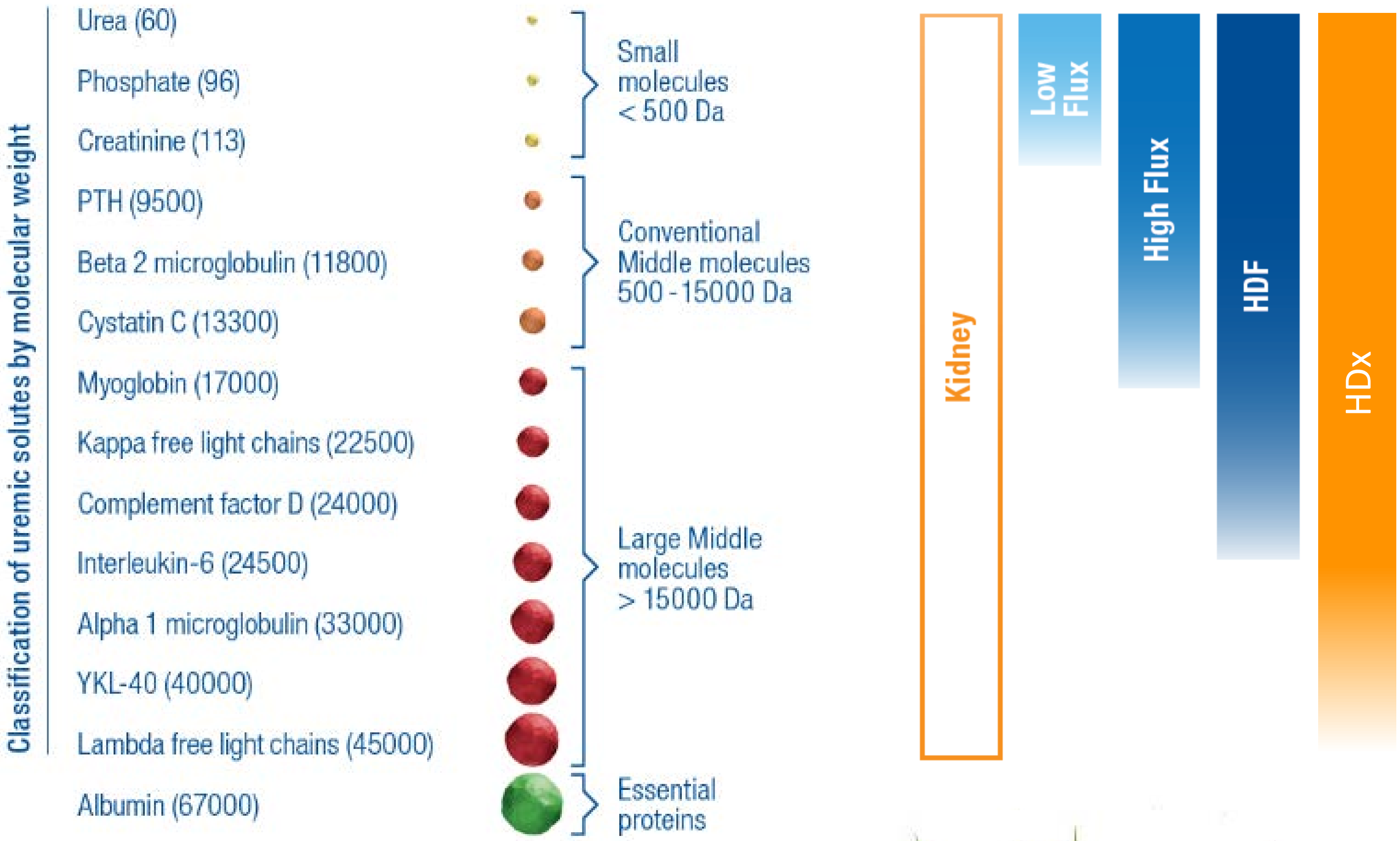
Published online: May 10, 2017

# The Rise of Expanded Hemodialysis

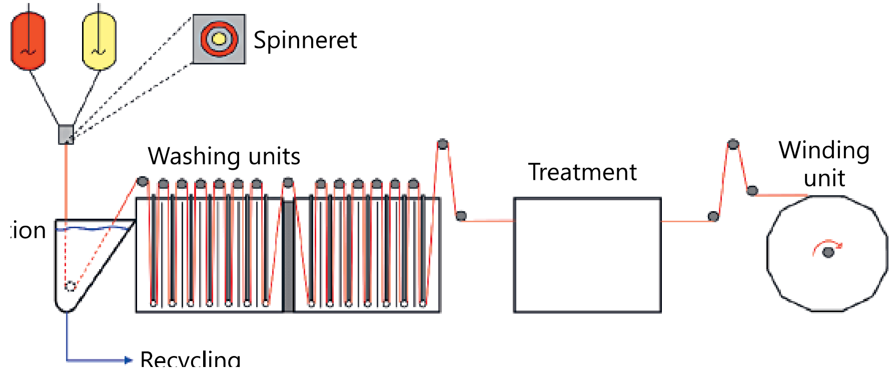
Claudio Ronco[a, b]

[a]Department of Nephrology Dialysis and Transplantation, St. Bortolo Hospital, and [b]International Renal Research Institute, Vicenza, Italy

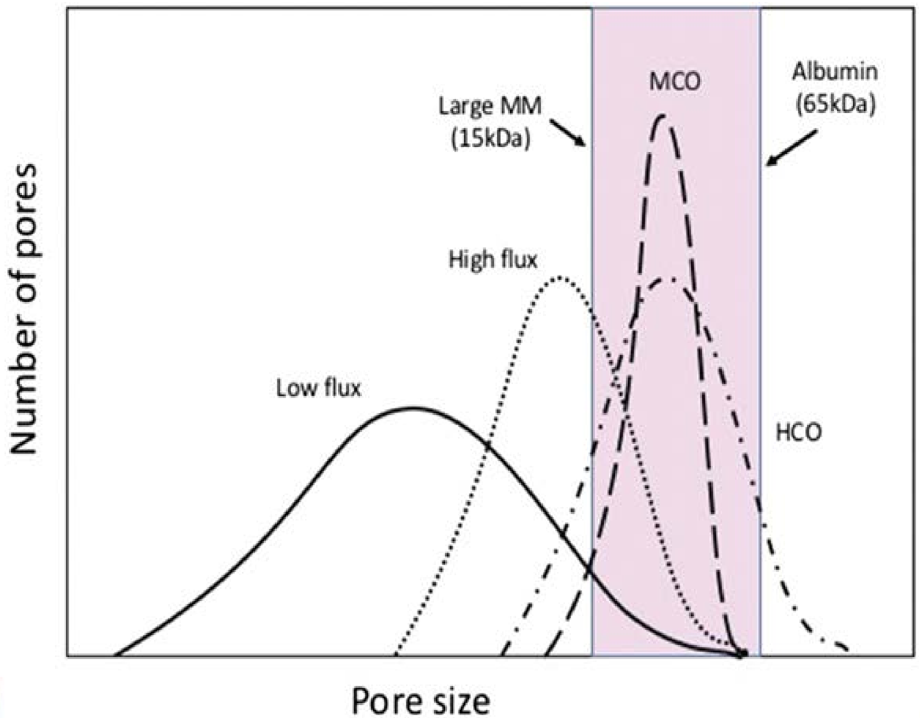
# HDx: a step closer to the native kidney



# MCO MEMBRANES




Ronco C (ed): Expanded Hemodialysis – Innovative Clinical Approach in Dialysis. Contrib Nephrol. Basel, Karger, 2017, vol 191, pp 100–114




Wolley et al. Large Middle Molecules and Hemodialysis. Clin J Am Soc Nephrol 13, May, 2018

# HDx: Medium Cut-off Membranes performance

Nephrol Dial Transplant (2017) 32: 165–172
doi: 10.1093/ndt/gfw310
Advance Access publication 1 September 2016

ndt
Nephrology Dialysis Transplantation

*Original Articles*

## Performance of hemodialysis with novel medium cut-off dialyzers

Alexander H. Kirsch[1], Raphael Lyko[2], Lars-Göran Nilsson[3], Werner Beck[4], Michael Amdahl[5], Petra Lechner[6], Andreas Schneider[2], Christoph Wanner[2], Alexander R. Rosenkranz[1] and Detlef H. Krieter[2]

Nephrol Dial Transplant (2016) 0: 1–8
doi: 10.1093/ndt/gfw310

*Original Article*

# Performance of hemodialysis with novel medium cut-off dialyzers

- **PerCOM:** two prospective, open-label, controlled, randomized, crossover pilot studies, 39 prevalent hemodialysis (HD) patients were studied in four dialysis treatments
- Single Treatment Performance Data Obtained with MCO Membranes
- **Primary outcome** was lambda free light chain (λFLC) overall clearance.
- **Secondary outcomes** included overall clearances and pre-to-post-reduction ratios of middle and small molecules, and safety of MCO HD treatments.

Kirsch AH et al, NDT 2017;32:165-172

Nephrol Dial Transplant (2016) 0: 1–8
doi: 10.1093/ndt/gfw310

ndt
Nephrology Dialysis Transplantation

*Original Article*

# Performance of hemodialysis with novel medium cut-off dialyzers

| | PerCom 1<br>NCT02377570 | PerCom 2<br>NCT02377622 |
|---|---|---|
| **Sites / PI** | | |
| | Graz, Austria<br>Prof. A. Rosenkranz<br>Bruck an der Mur<br>Dr. P. Lechner | Elsenfeld, Germany<br>Prof. D. Krieter |
| **Study design** | | |
| | Cross-over comparison of four dialyzers used in single mid-week treatments, in randomized order | |
| **Studied dialyzers** | | |
| | Theranova 400 – HD | Theranova 400 – HD |
| | FX Cordiax 80 – HD | FX Cordiax 800 – HDF |
| | MCO prototype BB – HD | FX Cordiax 80 – HD |
| | MCO prototype CC – HD | MCO prototype BB – HD |

Adapted from Kirsch AH et al, NDT 2017;32:165-172

**Table 1. Characteristics of dialysis membranes in study dialyzers**

| | Lot no. | Inner diameter (μm) | Wall thickness (μm) | Membrane polymer[a] | Effective surface area[a] ($m^2$) | UF coefficient[a] (mL/h/mmHg) |
|---|---|---|---|---|---|---|
| MCO AA | 4-806 | 180 ± 2 | 36 ± 1 | Polyarylethersulfone-PVP blend | 1.7 | 48 |
| MCO BB | 4-807 | 180 ± 2 | 35 ± 1 | Polyarylethersulfone-PVP blend | 1.7 | 52 |
| MCO CC | 4-808 | 180 ± 2 | 35 ± 1 | Polyarylethersulfone-PVP blend | 1.7 | 49 |
| FX CorDiax 80 | VKU07200 | 175 ± 3 | 38 ± 2 | Polysulfone-PVP blend | 1.8 | 64 |
| FX CorDiax 800 | VIF15100 | 199 ± 3 | 44 ± 2 | Polysulfone-PVP blend | 2.0 | 62 |

Mean ± SD.

[a]According to manufacturer's instruction for use.

PVP, polyvinylpyrrolidone; UF, ultrafiltration.

Nephrol Dial Transplant (2016) 0: 1–8
doi: 10.1093/ndt/gfw310

*Original Article*

# Performance of hemodialysis with novel medium cut-off dialyzers

| | PerCom 1 | PerCom 2 |
|---|---|---|
| Patients enrolled | N = 19 | N = 20 |
| Age (years) | 55 ±13 | 65 ±12 |
| Gender (M/F) | 12 / 7 | 16 / 4 |
| Body weight (kg) | 87.2 ±20.1 | 76.9 ±18.1 |
| Hematocrit (%) | 33.5 ±2.7 | 34.7 ±3.3 |
| Treatment data | N = 19 | N = 19 |
| $Q_B$ (ml/min) | 301 ±22 | 400 ±0 |
| $Q_D$ (ml/min) | 500 | 600[1] |
| Dialysis time (hours) | 4.0 ±0 | 4.4 ±0.3 |
| Blood volume processed (L) | 69 ±5 | 101 ±5 |
| UF (L) | 2.1 ±1.0 | 2.6 ±1.1 |
| HDF infusion volume | - | 21.4 ±1.1 |

HDF Convective Volume: 24 L

[1] In HDF the total dialysis fluid preparation flow was set at 700 ml/min, resulting in an effective QD through the dialyzer of close to 600 ml/min

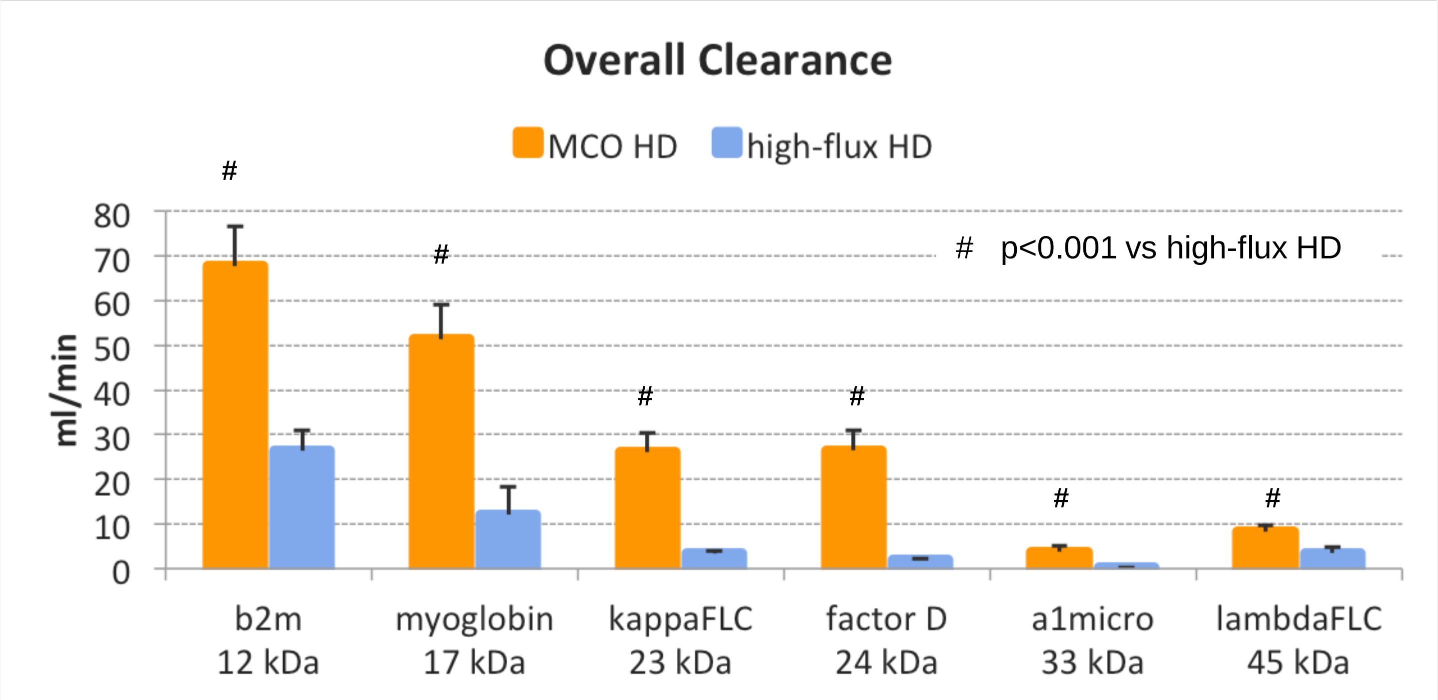
Aadapted from Kirsch AH et al, NDT 2017;32:165-172

Nephrol Dial Transplant (2016) 0: 1–8
doi: 10.1093/ndt/gfw310

PerCom 1

*Original Article*

# Performance of hemodialysis with novel medium cut-off dialyzers




N = 19
$Q_B$ = 301 ±22 ml/min
T = 4.0 h

MCO HD = THERANOVA 400 dialyzer

high-flux HD = HD by FX CORDIAX 80 dialyzer

Bars indicate mean and SD

Statistics: mixed model with fixed effects of period and dialyzer, and the random effect of subject

Adapted from Kirsch AH et al, NDT 2017;32:165-172
Baxter Clinical Study Report: 1407-003

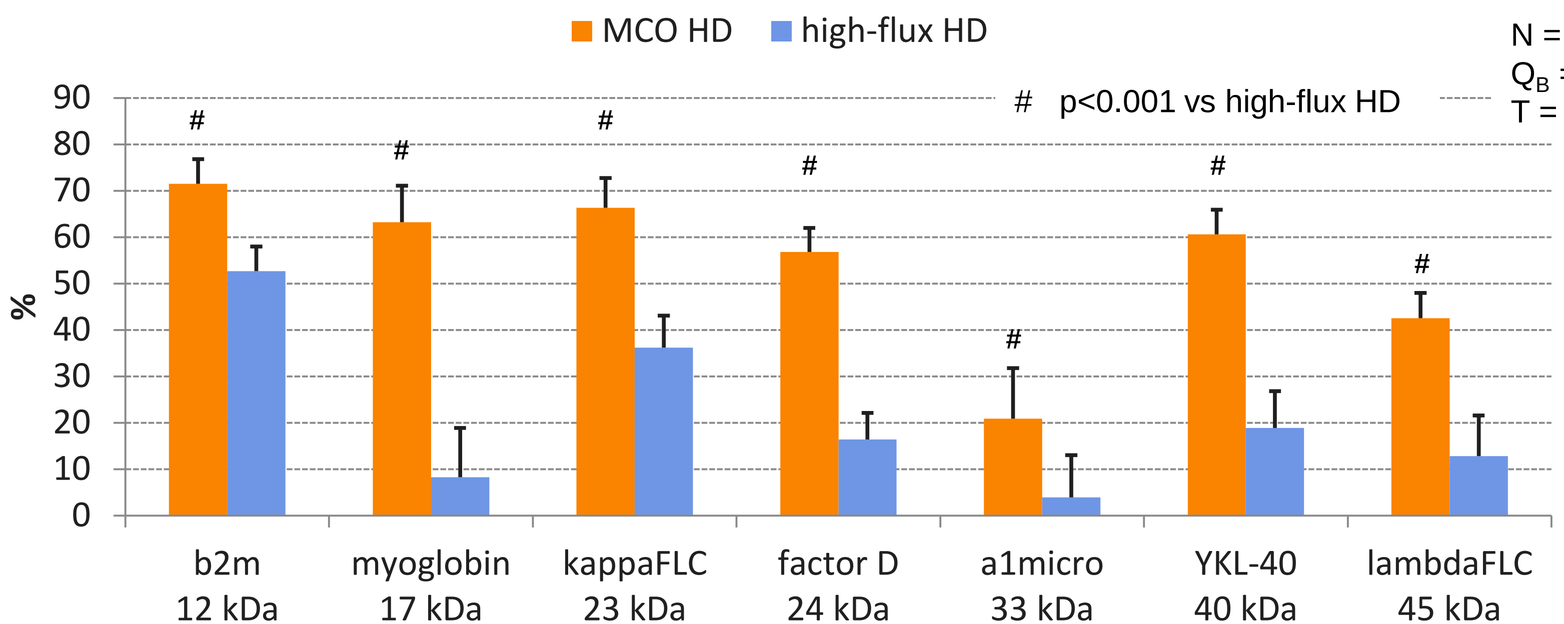
Nephrol Dial Transplant (2016) 0: 1–8
doi: 10.1093/ndt/gfw310

PerCom 1

*Original Article*

## Performance of hemodialysis with novel medium cut-off dialyzers

### Pre- to post-dialysis reduction in plasma level




N = 19
$Q_B$ = 301 ±22 ml/min
T = 4.0 h

MCO HD = THERANOVA 400 dialyzer

high-flux HD = HD by FX CORDIAX 80 dialyzer

Bars indicate mean and SD

Post-dialysis data corrected for hemoconcentration

Statistics: mixed model with fixed effects of period and dialyzer, and the random effect of subject

Adapted from Kirsch AH et al, NDT 2017;32:165-172
Baxter Clinical Study Report: 1407-003

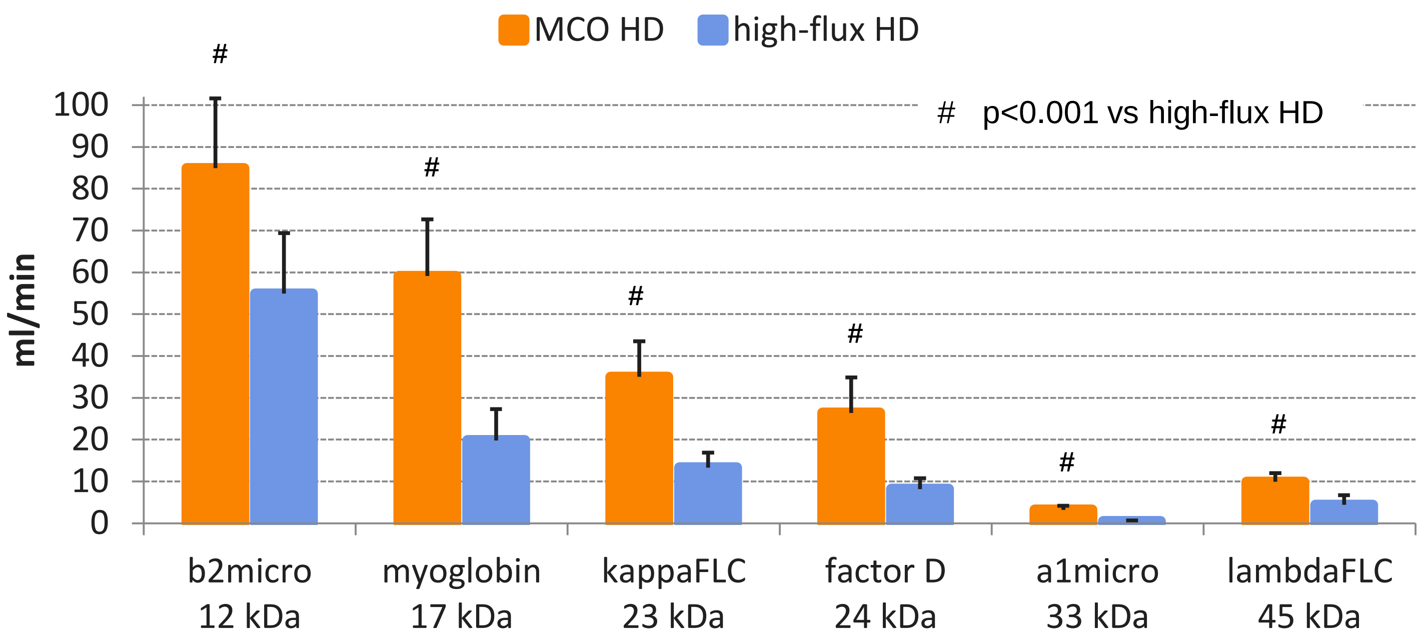
Nephrol Dial Transplant (2016) 0: 1–8
doi: 10.1093/ndt/gfw310

PerCom 2

*Original Article*

# Performance of hemodialysis with novel medium cut-off dialyzers

## Overall clearance




N = 19
$Q_B$ = 400 ml/min
T = 4.4 ±0.3 h

MCO HD = THERANOVA 400 dialyzer

high-flux HD = HD by FX CORDIAX 80 dialyzer

Bars indicate mean and SD

Statistics: mixed model with fixed effects of period and dialyzer, and the random effect of subject

Adapted from Kirsch AH et al, NDT 2017;32:165-172
Baxter Clinical Study Report: 1407-001

Nephrol Dial Transplant (2016) 0: 1–8
doi: 10.1093/ndt/gfw310

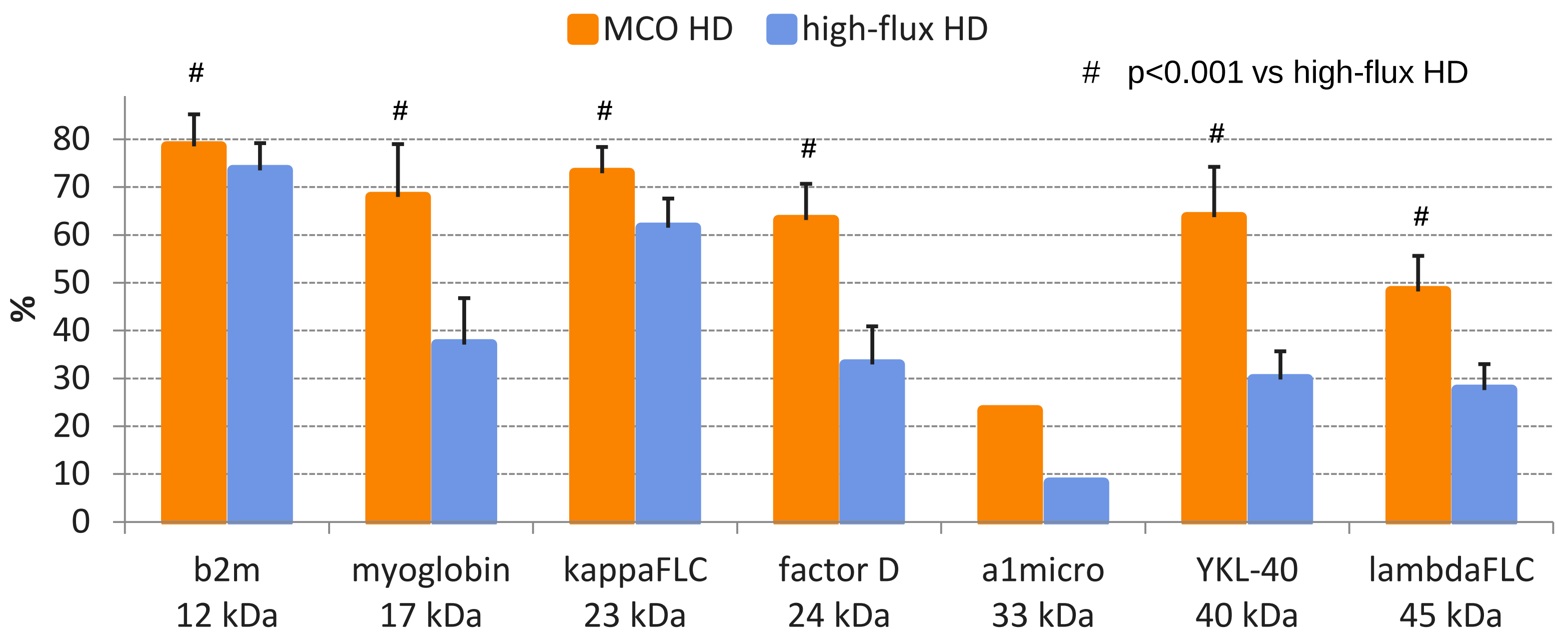
ndt

PerCom 2

*Original Article*

# Performance of hemodialysis with novel medium cut-off dialyzers

## Pre- to post-dialysis reduction in plasma level




N = 19
$Q_B$ = 400 ml/min
T = 4.4 ±0.3 h

MCO HD = THERANOVA 400 dialyzer
high-flux HD = HD by FX CORDIAX 80 dialyzer
Bars indicate mean and SD (median for a1micro)
Post-dialysis data corrected for hemoconcentration
Statistics: mixed model with fixed effects of period and dialyzer, and the random effect of subject

Adapted from Kirsch AH et al, NDT 2017;32:165-172
Baxter Clinical Study Report: 1407-001

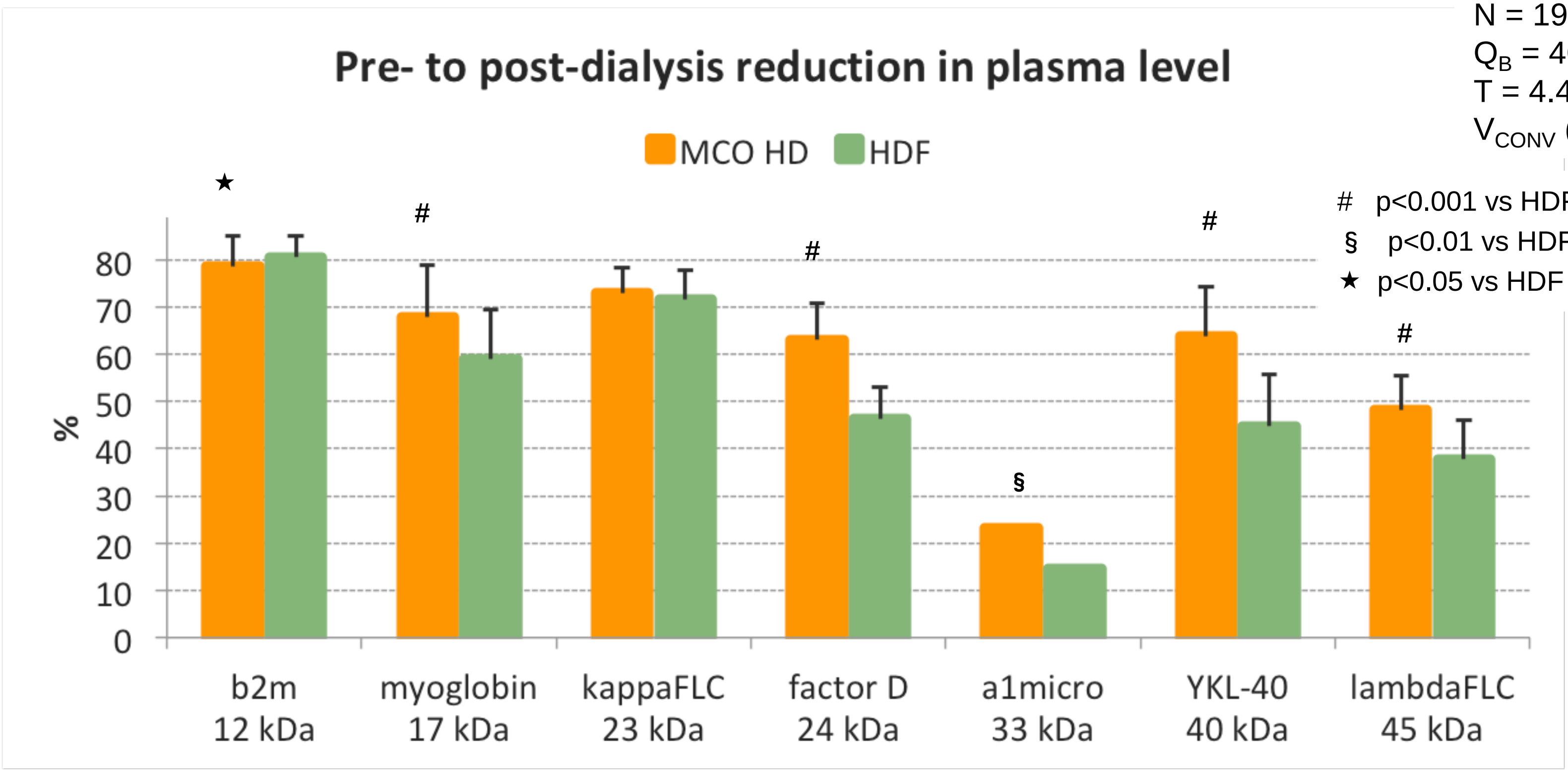
Nephrol Dial Transplant (2016) 0: 1–8
doi: 10.1093/ndt/gfw310

PerCom 2

*Original Article*

# Performance of hemodialysis with novel medium cut-off dialyzers

N = 19
$Q_B$ = 400 ml/min
T = 4.4 ±0.3 h
$V_{CONV}$ (HDF) = 24 L




\# p<0.001 vs HDF
§ p<0.01 vs HDF
★ p<0.05 vs HDF

MCO HD = THERANOVA 400 dialyzer
HDF = postdilution by FX CORDIAX 800 dialyzer
Bars indicate mean and SD (median for a1micro)
Post-dialysis data corrected for hemoconcentration
Statistics: mixed model with fixed effects of period and dialyzer, and the random effect of subject

Adapted from Kirsch AH et al, NDT 2017;32:165-172
Baxter Clinical Study Report: 1407-001

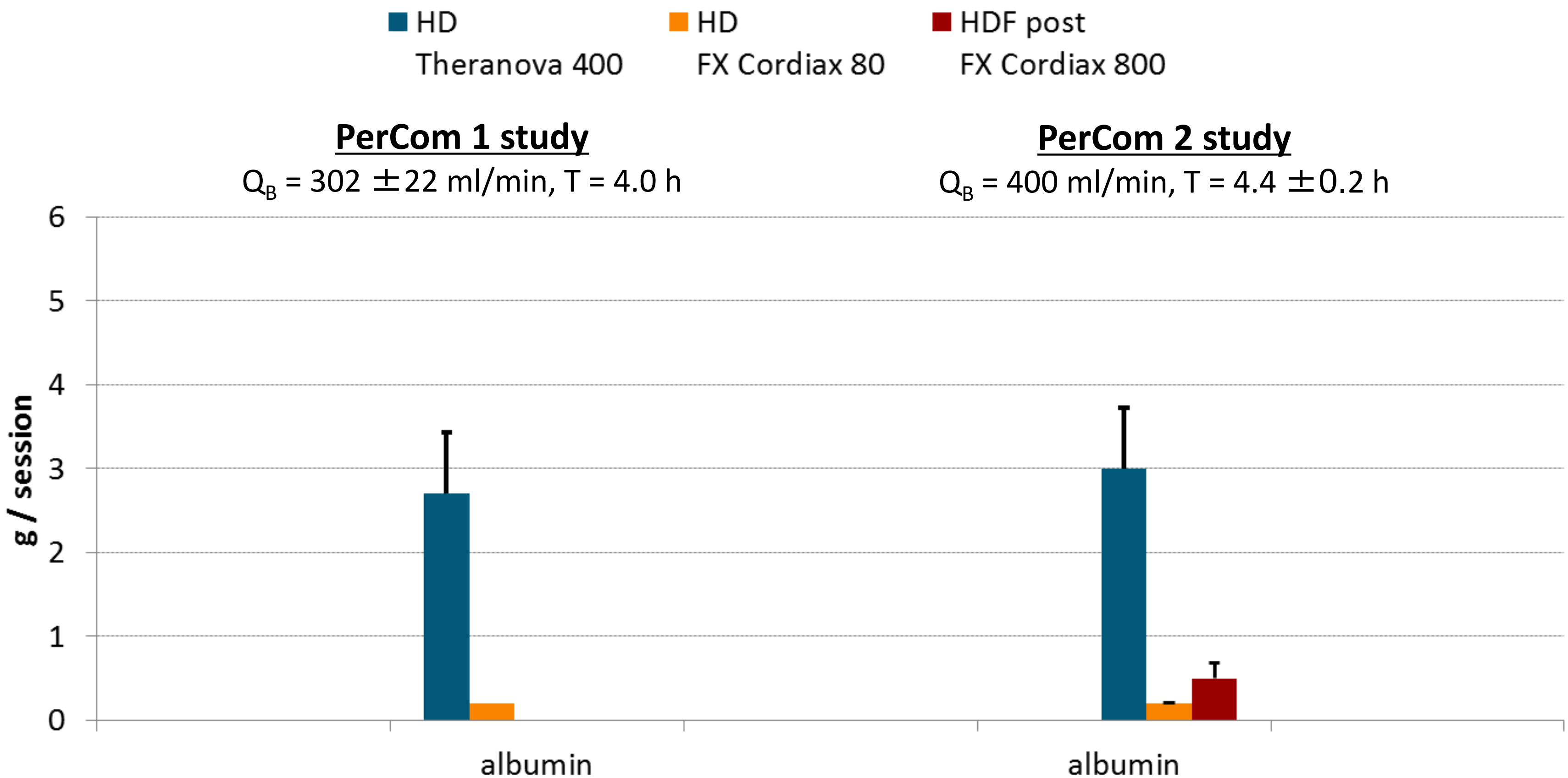
Nephrol Dial Transplant (2016) 0: 1–8
doi: 10.1093/ndt/gfw310

ndt
Nephrology Dialysis Transplantation

*Original Article*

Performance of hemodialysis with novel medium cut-off dialyzers

## Amount of albumin found in spent dialysate




Bars indicate mean and SD.

Kirsch AH et al, NDT 2017;32:165-172

Nephrol Dial Transplant (2016) 0: 1–8
doi: 10.1093/ndt/gfw310

*Original Article*

## Performance of hemodialysis with novel medium cut-off dialyzers

- MCO HD removes a wide range of middle molecules more effectively than high-flux HD, with the trade-off of increased albumin removal, compared to high-flux HD and HDF

- MCO HD also exceeds the performance of high-volume HDF for larger middle molecules, particularly λFLC

- Importantly, MCO HD can be applied to maintenance HD patients, in whom high volume HDF may not be used or is not available.

**Για high volume HDF χρειάζονται υψηλές ροές αντλίας αίματος**

Kirsch AH et al, NDT 2017;32:165-172

ckj

Clinical Kidney Journal, 2018, 1–5

doi: 10.1093/ckj/sfy004
Original Article

ORIGINAL ARTICLE

# Evaluation of the efficacy of a medium cut-off dialyser and comparison with other high-flux dialysers in conventional haemodialysis and online haemodiafiltration

**Table 4.** Comparison of RR with each molecule using HF HD with FX80 dialyser, HD with MCO Theranova dialyser and OL-HDF using FX1000 dialyser

| Substance | FX80 HD | Theranova HD | FX1000 OL-HDF | P-value |
|---|---|---|---|---|
| Urea | 82.3 (4.39) | 83.5 (7.15) | 85.4 (3.91) | ns |
| Creatinine | 74.8 (4.92) | 75.7 (7.47) | 77.4 (5.90) | ns |
| Phosphate | 58.8 (10.63) | 60.5 (11.62) | 61.4 (11.62) | ns |
| β2-microglobulin | 69.7 (6.57) | 74.7 (8.09)* | 81.2 (4.29)* | <0.001 |
| Cystatin C | 63.8 (4.79) | 71.6 (7.45)** | 78.9 (4.87)* | <0.001 |
| Myoglobin | 34.3 (7.88) | 62.5 (8.66)* | 72.4 (7.31)* | <0.001 |
| Prolactin | 32.8 (9.79) | 60 (8.20)* | 69.2 (9.13)* | <0.001 |
| α1-glycoprotein | −0.1 (6.85) | 2.8 (18.79)** | 2.4 (7.98)* | 0.02 |

All values presented as mean (SD).
*$P < 0.001$ versus HD.
**$P < 0.05$ versus HD.
ns, non-significant.

# Comparison of hemodialysis with medium cut-off dialyzer and on-line hemodiafiltration on the removal of small and middle size molecules

Mohamed Belmouaz, Jeremy Diolez, Marc Bauwens, Laure Ecotiere, Estelle Desport, Frank Bridoux. Department of Nephrology, CHU Poitiers, Université de Poitiers, France

**Introduction :** Theranova™ (polyarylethersufone/polyvinypyrrolidone, Gambro ) is a novel generation medium cut-off (MCO) dialyzer designed to increase the removal of molecules over 25 kDa [1]. Recent clinical data on the use of MCO dialyzer in hemodialysis (MCO-HD) patients have shown efficient removal of β2-microglobulin, myoglobin, kappa and lambda free light chains, Complement factor D and alpha1 microglobulin [2]. We retrospectively compared removal of small and middle size molecules and nutritional parameters over a 6-month period of high-flux ol-HDF followed by 6 months of HD with Theranova-500™.

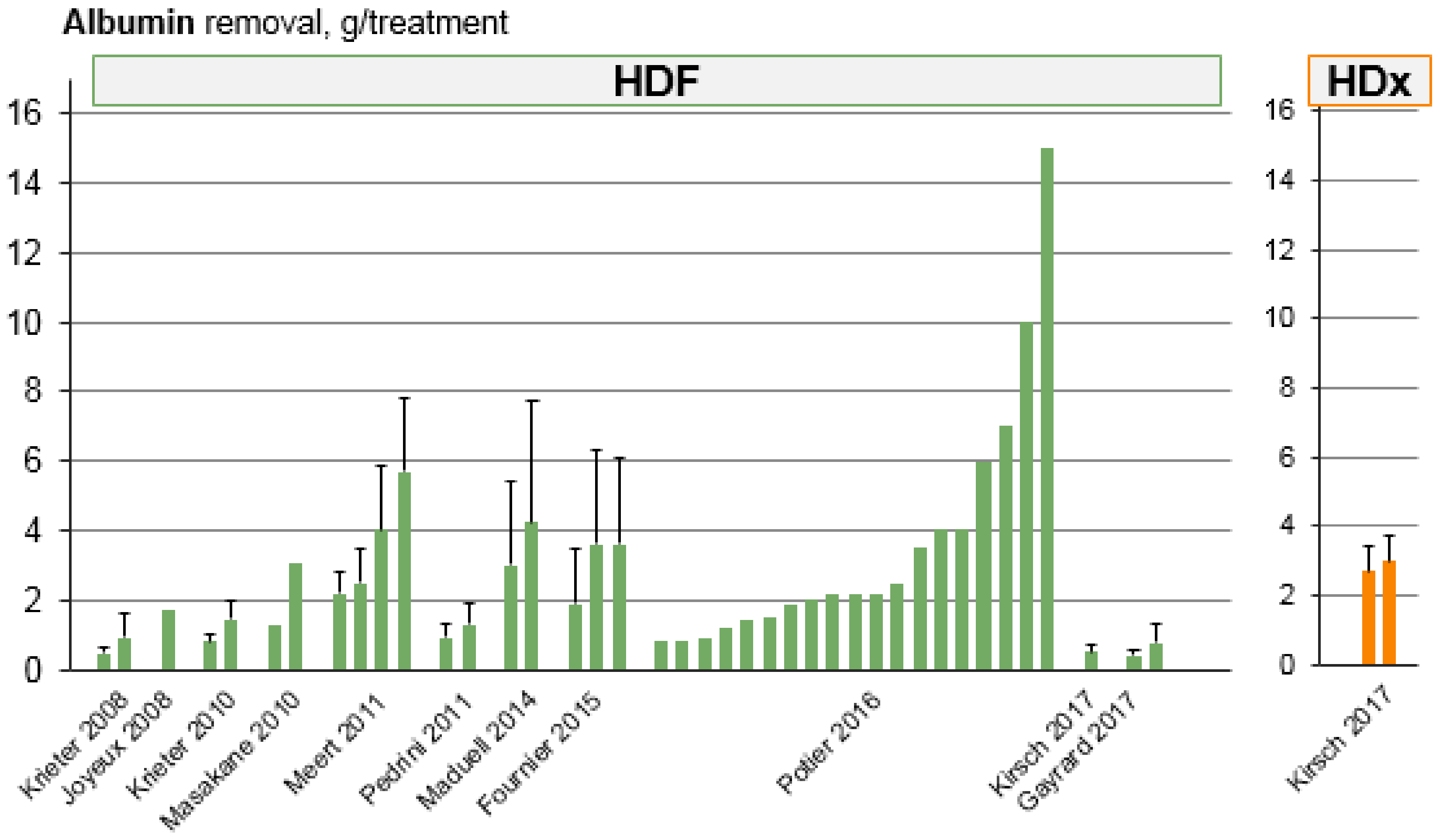
**Methods :** Ten stable patients established on post-dilution ol-HDF using high-flux dialyzer (table 1) for at least 6 months in our hemodialysis department, then switched to HD with the Theranova-500™ MCO dialyzer for a 6 month period were retrospectively studied. Blood samples were taken routinely every two months at the first mid-week dialysis session. The following measurements were performed: pre and post-dialysis urea, creatinine, β2-microgloblin and myoglobin serum levels, and pre-dialysis albumin, prealbumin and CRP serum levels.

**Table 3.** Biological, nutritional and inflammatory parameters

| | High-flux ol-HDF | MCO-HD | p |
|---|---|---|---|
| Albumin (g/l) * | 37.8 (5) | 38 (6.4) | 0.29 |
| Prealbumin (mg/l) * | 0.28 (0.08) | 0.26 (0.14) | 0.25 |
| nPCR * | 0.9 (0.3) | 1 (0.4) | 0.95 |
| CRP (mg/l) * | 8 (9.0) | 7 (6.5) | 0.35 |
| β2-microglobulin (mg/l) | | | |
| Pre * | 27.5 (4) | 28 (3.0) | 0.63 |
| Post * | 5.6 (1.6) | 6.2 (0.9) | 0.56 |
| Myoglobin (µg/l) | | | |
| Pre * | 164 (81) | 184 (151) | 0.67 |
| Post * | 79 (51) | 76 (64) | 0.72 |

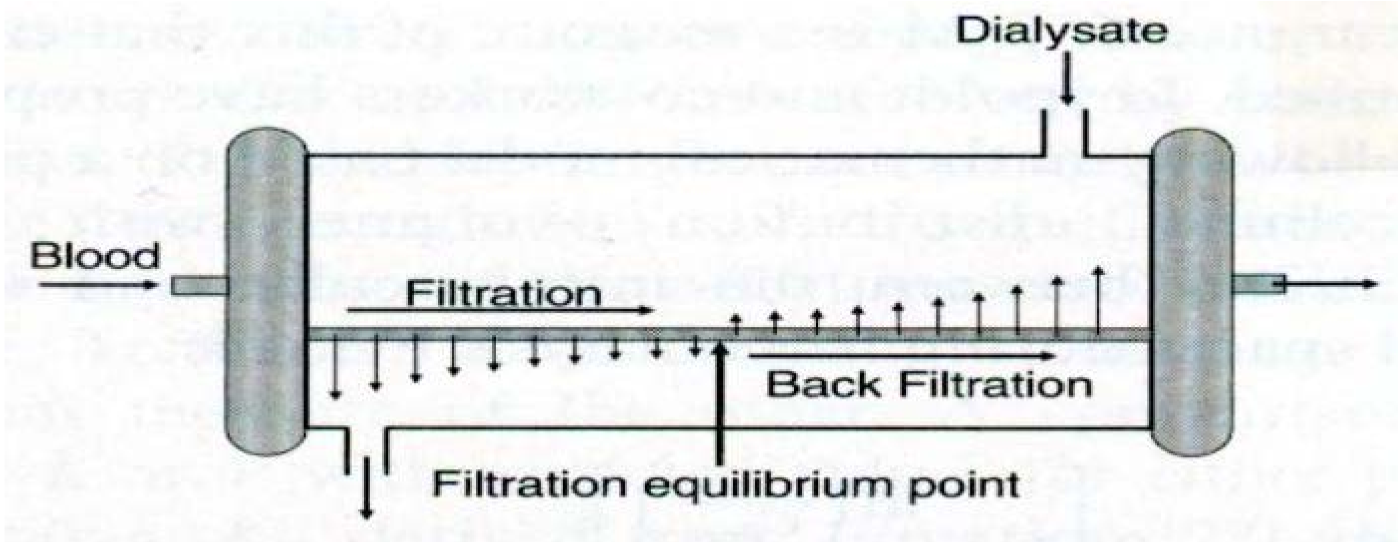
* Data are expressed as median (IQR)

# Η απώλεια αλβουμίνης αποτελεί πρόβλημα στην HDx ;




HDF data are obtained in different studies using a variety of high-flux dialyzers, different dilution modes (post-, pre-, mid-), and different convective flow rates

# BACKFILTRATION

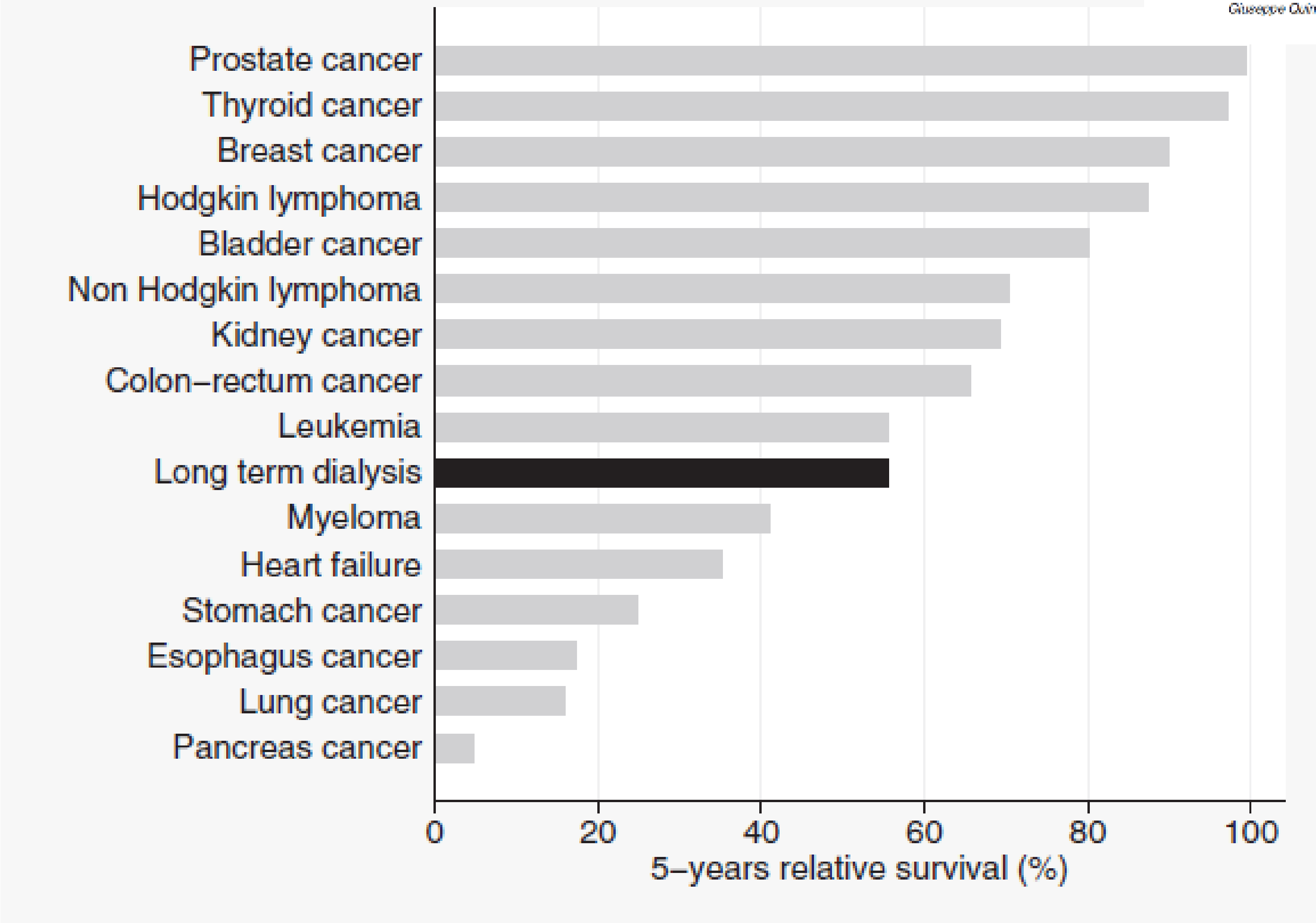



Δεν υπάρχουν ενδείξεις για αυξημένη διαπερατότητα ενδοτοξινών και επιμόλυνση στο αιματικό διαμέρισμα του φίλτρου, όπως προκύπτει απο πειρατικά μοντέλα


Schepers E, Glorieux G, Eloot S, Hulko M, Boschetti-de-Fierro A, Beck W, Krause B, Van Biesen W: Mp537: Does increasing mem- brane pore size affect endotoxin permeability? A novel dialysis simulation set-up. Nephrol Dial Transplant 32: iii625–iii626, 2017

Hulko M, Gekeler A, Koch I *et al*. Dialysis membrane pore size does not determine LPS retention. *Nephrol Dial Transplant* 2015; 30(Suppl 3): iii244.

# Μπορούμε να βελτιώσουμε την επιβίωση των ΑΜΚ ασθενών με HDx ?




AJKD
Original Investigation

**Survival in Patients Treated by Long-term Dialysis Compared With the General Population**

*Maurizio Nordio, MD, MSc(Epid),[1] Aurelio Limido, MD,[2] Umberto Maggiore, MD, PhD,[3] Michele Nichelatti, BSc, PhD,[4] Maurizio Postorino, MD,[5] and Giuseppe Quintaliani, MD,[6] on behalf of the Italian Dialysis and Transplantation Registry**

# Διευρυμένη ΑΜΚ (HDx therapy)-Κλινικές μελέτες

| Public registration | Study title | Study PI |
|---|---|---|
| ACTRN12616000804482<br>Completion 2018 | REMOVAL-HD<br>A tRial Evaluating Mid cut-Off Value membrane clearance of Albumin and Light chains in HaemoDialysis patients | Colin Hutchison et al., multi-center, ANZ |
| DRKS00012359<br>Completion 2018 | REMOC<br>REmoval of middle MOlecules using medium Cut-off membranes in hemodialysis mode versus high-flux membranes in post-dilutional on-line hemodiafiltration mode | Alexander Rosenkranz, Graz, Austria |
| NCT03270371<br>Completion date Feb 2019 | MCO-IF<br>Medium-term Modulation of the Inflammatory Profile by Medium Cut Off Membranes in Patients With End Stage Renal Disease | Christoph Schmaderer, Munich, Gerrmany |
| NCT03211676<br>Completion date Dec 2017 | Comparison of Hemodialysis With Medium Cut-off Dialyzer (Theranova) and High Flux Dialyzer on Removal of Small and Middle Size Molecules, Inflammatory Parameters and Oxidative Stress. An Open Cross Over Randomized Study | Mohamed Belmouaz, Poitiers, France<br>**Finished** |
| NCT03104166<br>Completion date Dec 2018 | ModuVas<br>Modulation of Vascular Calcification in Chronic Dialysis Patients | Daniel Zickler, Berlin, Germany |
| NCT03137056<br>Completion date April 2018 | DIALOMIC<br>Characterization of Proteins and Forms of Albumin Removal Capacities of the Theranova Membrane by Innovating Proteomic Investigations | Laurent Juillard, Lyon, France |
| NCT03169400<br>Completion date Dec 2018 | Molecular and cellular mechanism of vascular ageing in CKD: role of Theranova dialyzer on mineral metabolism disorder, oxidative stress, and vascular calcification | Mario Cozzolino, Milan, Italy |
| NCT03274518<br>Completion date April 2018 | Expanded Hemodialysis Versus Online Hemodiafiltration: a Pilot Study on Intradialytic Hemodynamics and Fluid Status | Bruno Caldin da Silva, Sao Paulo, Brazil |

# Συμπεράσματα

- Η διευρυμένη ΑΜΚ (HDx) αποτελεί μια προηγμένη θεραπεία που μπορεί πλέον να εφαρμοσθεί,
- χάρις την δημιουργία των MCO μεμβρανών,
- ακόμα και σε μονάδες ΤΝ χωρίς ειδικό τεχνολογικό εξοπλισμό
- Προσφέρει απόδοση παρόμοια με την high volume HDF και ακόμα καλυτερη στην κάθαρση μεγαλύτερων ΜΒ ουραιμικών τοξινών με τις συνθήκες της απλής ΑΜΚ
- Χωρίς επιπλέον κόστος
- Περισσότερες μελέτες θα χρειασθούν για να διαπιστωθεί αν η εφασρμογή της HDx θα βελτιώσει την επιβίωση των ΑΜΚ ασθενών
- HDx: ένα βήμα πιο κοντά στο τρόπο λειτουργίας του φυσικού νεφρού