Hemodiafiltration versus Mixed Hemodiafiltration: What’s Place?

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Speaker name: Prof. Bernard Canaud

☐ I have the following potential conflicts of interest to report:

☐ Consulting

☒ Employment in industry (FMC)

☐ Shareholder in a healthcare company

☐ Owner of a healthcare company

☐ Other(s)

☐ I do not have any potential conflict of interest
Outlook of the Presentation

1. What is optimal in convective therapies?
   - Convective dose: postdilution HDF as reference
2. What’s matter in HDF?
   - Dilution mode: Post - Pre - Mixed - Mid
3. Why mixed-HDF is necessary?
   - Medical & engineering rationale
4. How to use mixed-HDF?
   - Technical aspects
   - Nursing & Doctor perspectives
5. What indications?
6. What results?
7. Take home message
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From Dialyzer Clearance to Body Mass Transfer
Effective Solute Mass Removal per Session

- **Solute Dialyzer Clearance**
  - $K_D \Sigma D+C+A$ (ml/min)
  - Solute Characteristics
    - Membrane Permeability
    - Surface Area - Filter Design
  - Operational Conditions
    - Blood Flow
    - Dialysate Flow
    - Ultrafiltration Flow
  - Patient Characteristics
  - Practice Patterns

- **Solute Body Clearance**
  - $K_B$ (mmol/min)
  - Effective Treatment Time
  - Frequency Time Duration
  - Metabolic profile
  - Vascular access performances
  - Treatment tolerance, Weight loss...
  - Effective flow/time/dialysate flow/substitution flow
  - Recirculation...

- **Solute Mass Transfer**
  - $K_B.C_s$ (mmol/sem/wk)
  - Diffusive + Convective Dose
From Mass Transfer to Patient Needs
RRT Adequacy: Effective Solute Mass Removal per Week

HD HD HD HD

Intermittent treatment

RRT Efficacy
Homeostasis
Patient’s Needs
Cubic Spline Analysis of Relative Survival Rate Vs Convection Volume Non Adjusted

HRs for CardioVascular Mortality In Patients Receiving HDF Versus HD, Overall and in Subgroups

- Overall: HR = 0.77 (0.61, 0.97) with a 23% reduction.
- Sex:
  - Men: HR = 0.88 (0.66, 1.17) with a 41% reduction.
  - Women: HR = 0.59 (0.40, 0.89) with a 30% reduction.
- Age:
  - <65 yrs: HR = 1.11 (0.76, 1.62) with a 31% reduction.
  - >= 65 yrs: HR = 0.69 (0.52, 0.90) with a 30% reduction.
- Diabetes:
  - No: HR = 0.72 (0.53, 0.97) with a 29% reduction.
  - Yes: HR = 0.84 (0.58, 1.21) with a 30% reduction.
- History of CVD:
  - No: HR = 0.82 (0.61, 1.09) with a 24% reduction.
  - Yes: HR = 0.70 (0.50, 0.98) with a 26% reduction.
- Albumin:
  - < 4 g/dL: HR = 0.76 (0.57, 1.03) with a 27% reduction.
  - >= 4 g/dL: HR = 0.76 (0.56, 1.03) with a 28% reduction.
- Dialysis vintage:
  - < 30 months: HR = 0.79 (0.56, 1.11) with a 25% reduction.
  - >= 30 months: HR = 0.73 (0.53, 1.01) with a 26% reduction.
- Vascular access:
  - Fistula: HR = 0.78 (0.61, 1.00) with a 24% reduction.
  - Other: HR = 0.77 (0.42, 1.42) with a 25% reduction.

2793 prevalent ESKD pts

Simulated Benefits of Convective Volume on Relative Risk of Mortality in CKD Patients

Imamovic G et al, ‘Rational for Improved Patients' Survival on Hemodiafiltration’ in InTech Chapter, 2016 In Press
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**Post-dilution Hemodiafiltration**

\[ Q_{UF} = \text{Ultrafiltration Rate} \]
\[ Q_{SUB} = \text{Substitution Rate} \]
\[ K_{UF} = \frac{\text{WL}}{t_{HD}} \text{ Weight Loss} \]
\[ Q_F = \text{Total Ultrafiltration Rate} \]
\[ DF = \text{Dilution Factor} \]
\[ S = \text{Sieving Coefficient} \]

\[ Q_{B_{in}} = \text{Blood Flow In} \]
\[ Q_{B_{out}} = \text{Blood Flow Out} \]
\[ Q_{D_{in}} = \text{Dialysate Flow In} \]
\[ Q_{D_{out}} = \text{Dialysate Flow Out} \]

Sieving Coefficient = \( \frac{C_{S_b}}{C_{S_f}} \)

Different Modalities of HDF
Defined from Substitution Sites

Post-Dilution HDF

Pre-Dilution HDF

Mixed-Dilution HDF

Mid-Dilution HDF
Postdilution Hemodiafiltration
Flow and Fluid Transfer

$Q_{b_{in}} = 400$

$Q_{D_{out}} = 500$

$Q_{D_{in}} = 500$

$Q_{SUB} = 100$

$Q_{b_{in}} = 400$

$Q_{D_{out}} = 500$

$Q_{D_{in}} = 500$

$Q_{b_{in}} = 400$

$Q_{D_{out}} = 500$

$Q_{D_{in}} = 500$

$Q_{SUB} = 100$

$Q_{D_{in}} = 500$

$Q_{D_{out}} = 500$

$Q_{b_{in}} = 400$

$Q_{D_{out}} = 500$

$Q_{D_{in}} = 500$

$Q_{SUB} = 100$

$Q_{D_{in}} = 500$

$Q_{D_{out}} = 500$

$Q_{b_{in}} = 400$

$Q_{D_{out}} = 500$

$Q_{D_{in}} = 500$

$Q_{SUB} = 100$

FF = 110/400 = 27.5%
**Postdilution Hemodiafiltration**

$$K_D = \frac{1 - e^{K_d A [(Q_b - Q_D)/(Q_b - Q_D)]}}{(1/Q_b) - (1/Q_d) \times e^{K_d A [(Q_b - Q_D)/(Q_b - Q_D)]}}$$

**Diffusive Clearance, KD**

$$K_d = \frac{Q_D \times [Q_b - Q_D]}{Q_b - Q_D^{out}}$$

$$K_f = \frac{Q_B \times [Q_b^{out} - Q_D]}{Q_b - Q_D^{out}}$$

$$T_{diff} = \frac{Q_b \times [Q_b^{out} - Q_D]}{Q_b - Q_D^{out}}$$

**Convective Clearance, KC**

$$K_C = \frac{Q_b - K_D}{Q_b} \times Q_f \times S$$

**Total Solute Clearance**

$$K_T = (K_D + K_C) \times DF$$

**Symbols and Equations**

- $Q_B^{in}$ = Blood Flow In
- $Q_B^{out}$ = Blood Flow Out
- $Q_D^{in}$ = Dialysate Flow In
- $Q_D^{out}$ = Dialysate Flow Out
- $K_D$ = Diffusive Clearance Coefficient
- $K_C$ = Convective Clearance Coefficient
- $Q_f$ = Total Ultrafiltration Rate
- $S$ = Sieving Coefficient
- $DF$ = Dilution Factor
- $K_{uf}$ = Ultrafiltration Rate
- $Q_{sub}$ = Substitution Rate
- $K_{uf}$ = Weight Loss

**References**

Postdilution Hemodiafiltration
Solute Profile & Convective Clearance

Total Solute Clearance
\[ K_T = (K_D + K_C) \times DF \]

DF = 400/400 = 1.0

FF = 110/400 = 27.5%

Solute Conc. (%)
Predilution Hemodiafiltration
Flow and Fluid Transfer

\[ \text{Q}_{\text{SUB}} = 100 \]
\[ \text{Q}_{\text{D}_{\text{out}}} = 500 \]
\[ \text{Q}_{\text{D}_{\text{in}}} = 500 \]

\[ \text{Q}_{\text{b}_{\text{in}}} = 400 \]
\[ \text{Q}_{\text{b}_{\text{out}}} = 390 \]

\[ \text{Q}_{\text{UF}} = 100 \] \[ K_{\text{UF}} = 10 \]

\[ \text{Total } \text{Q}_{\text{UF}} = 110 \]

\[ \text{FF} = \frac{110}{500} = 22.0\% \]

\( Q_{\text{IN}} = \) Blood Flow In
\( Q_{\text{OUT}} = \) Blood Flow Out
\( Q_{\text{D}_{\text{IN}}} = \) Dialysate Flow In
\( Q_{\text{D}_{\text{OUT}}} = \) Dialysate Flow Out
\( Q_{\text{UF}} = \) Ultrafiltration Rate
\( Q_{\text{SUB}} = \) Substitution Rate
\( K_{\text{UF}} = \) Weight Loss
**Predilution Hemodiafiltration**

Solute Profile & Convective Clearance

- $Q_{SUB} = 100$
- $Q_{Dout} = 500$
- $Q_{Din} = 500$
- $Q_{b_in} = 400$
- $Q_{b_out} = 390$

DF = $\frac{100}{400} = 0.25$

FF = $\frac{110}{500} = 22.0\%$

**Total Solute Clearance**

$$K_T = (K_D + K_C) \times DF$$

DF = 0.25

$$K_C = \frac{Q_b - K_D}{Q_b} \times Q_f \times S$$

$\uparrow Q_f$ & $\uparrow Q_{SUB}$
**Predilution Hemodiafiltration**

**Flow and Fluid Transfer Matching Post-HDF**

- $Q_{\text{SUB}} = 200$
- $Q_{\text{D}_{\text{out}}} = 500$
- $Q_{\text{D}_{\text{in}}} = 500$
- $Q_{\text{b}_{\text{in}}} = 400$
- $Q_{\text{B}_{\text{out}}} = 390$

**Flow Rates**

- $Q_{\text{UF}} = 200$
- $K_{\text{UF}} = 10$

**Total Flow Rate**

- $\text{Total } Q_{\text{UF}} = 210$

**Flow Fraction**

- $\text{FF} = 210/600 = 35.0\%$

**Symbols**

- $Q_{\text{B}_{\text{in}}}$ = Blood Flow In
- $Q_{\text{B}_{\text{out}}}$ = Blood Flow Out
- $Q_{\text{D}_{\text{in}}}$ = Dialysate Flow In
- $Q_{\text{D}_{\text{out}}}$ = Dialysate Flow Out
- $Q_{\text{UF}}$ = Ultrafiltration Rate
- $Q_{\text{SUB}}$ = Substitution Rate
- $K_{\text{UF}}$ = $WL/t_{\text{HD}}$, Weight Loss

**Formula**

- $\text{FF} = \frac{Q_{\text{UF}}}{Q_{\text{B}_{\text{in}}}}$
### Advantages & Disadvantages of Substitution Modalities

<table>
<thead>
<tr>
<th>Post-dilution HDF</th>
<th>Pre-dilution HDF</th>
<th>Mixed-dilution HDF</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pro:</strong></td>
<td><strong>Pro:</strong></td>
<td><strong>Pro:</strong></td>
</tr>
</tbody>
</table>
| • High solute clearance & removal  
  - Small, Middle & High MW solutes  
  • Reduce consumption of substitution volume | • Hemodilution  
  - Decrease protocrit & hematocrit  
  - Reduce viscosity & oncotic pressure  
  - Reduce fibers & membrane fouling  
  • Facilitate protein-bound solute clearance & removal  
  • Preserve hydraulic & solute membrane permeability  
  • Reduce membrane stress | • Avoid drawbacks of both post & pre-dilution methods |
| **Con:**          | **Con:**         | **Con:**           |
| • Hemoconcentration  
  - Increase protocrit & hematocrit  
  - Increase viscosity & oncotic pressure  
  - Fibers and membrane fouling  
  • Reduce hydraulic & solute membrane permeability  
  - Increase transmembrane pressure  
  - Fibers clotting  
  - Potential alarms  
  • Increase membrane stress  
  - Potential albumin leakage | • Reduce solute clearance & removal  
  - Small > Middle & High MW solutes  
  • Increase consumption of substitution volume | • Require specific hardware equipment  
  - Two infusion pumps  
  - Specific blood tubing set  
  • Require specific software & algorithm  
  - Accounting for hematocrit & protocrit changes  
  - Adjusting post/pre infusion ratio keeping transmembrane pressure in target  
  • Increase consumption of substitution volume |
Some Clinical Indicators for Choosing Best Substitution Modality

<table>
<thead>
<tr>
<th>Favorable to Post-HDF</th>
<th>Favorable to Pre or Mixed-HDF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good vascular access flow</td>
<td>Poor vascular access flow or veno-venous access</td>
</tr>
<tr>
<td>High blood flow</td>
<td>Low blood flow (&lt;300ml/min)</td>
</tr>
<tr>
<td>Hematocrit 30-35% or Hb 10-11g/dl</td>
<td>Hematocrit &gt;35% or Hb &gt;12g/dl</td>
</tr>
<tr>
<td>Albumin concentration (35-40g/l)</td>
<td>Albumin concentration &gt;40g/l</td>
</tr>
<tr>
<td>Standard weight loss or UFR &lt;15ml/Hr/kg</td>
<td>High weight loss or UFR &gt;15ml/Hr/kg</td>
</tr>
<tr>
<td>No inflammation, No active infection</td>
<td>Inflammation, Active infection</td>
</tr>
<tr>
<td>No paraproteinemia</td>
<td>Paraproteinemia</td>
</tr>
<tr>
<td>No hyperlipidemia, no hypertriglyceridemia</td>
<td>Hyperlipidemia, Hypertriglyceridemia</td>
</tr>
<tr>
<td>No hyperviscosity: fibrinogen &lt;3g/l, leukocytes &lt;5.10^3, Platelets &lt;150.10^3</td>
<td>Hyperviscosity</td>
</tr>
<tr>
<td>No clotting disorders</td>
<td>Clotting disorders</td>
</tr>
<tr>
<td>Unfavorable probing</td>
<td></td>
</tr>
</tbody>
</table>
Convective Dose Delivered in Postdilution HDF with Automatic Ultrafiltration Control (AutoSub⁺)

<table>
<thead>
<tr>
<th></th>
<th>FX Cordiax 60</th>
<th>FX Cordiax 600</th>
<th>FX Cordiax 800</th>
<th>FX Cordiax 100</th>
<th>ALL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (N)</td>
<td>325</td>
<td>2572</td>
<td>121</td>
<td>464</td>
<td>3315</td>
</tr>
<tr>
<td>Sessions (N)</td>
<td>10022</td>
<td>78177</td>
<td>3740</td>
<td>4888</td>
<td>106827</td>
</tr>
<tr>
<td>Age (years)</td>
<td>61.7 ± 14.8</td>
<td>64.8 ± 13.7</td>
<td>61.1 ± 12.6</td>
<td>63.5 ± 13.2</td>
<td>64.5 ± 13.7</td>
</tr>
<tr>
<td>Gender (Female, %)</td>
<td>47.2</td>
<td>38.5</td>
<td>17.9</td>
<td>34.9</td>
<td>39.2</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.2 ± 4.9</td>
<td>26.4 ± 5.5</td>
<td>30.1 ± 6.7</td>
<td>27.7 ± 6.3</td>
<td>24.4 ± 5.5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>FX Cordiax 60</th>
<th>FX Cordiax 600</th>
<th>FX Cordiax 800</th>
<th>FX Cordiax 100</th>
</tr>
</thead>
<tbody>
<tr>
<td>Substitution fluid volume (l/treatment)</td>
<td>22.6 ± 4.3</td>
<td>24.8 ± 4.6</td>
<td>25.0 ± 3.9</td>
<td>31.6 ± 7.2</td>
</tr>
<tr>
<td>Convection volume (l/treatment)</td>
<td>25.1 ± 4.1</td>
<td>27.3 ± 4.6</td>
<td>28.1 ± 3.9</td>
<td>37.0 ± 6.7</td>
</tr>
<tr>
<td>Mean Filtration Fraction (%)</td>
<td>29.6 ± 3.9</td>
<td>28.0 ± 3.8</td>
<td>30.3 ± 3.8</td>
<td>32.2 ± 4.4</td>
</tr>
<tr>
<td>Sessions with substitution fluid volume ≥21 L (%)</td>
<td>70.2</td>
<td>84.4</td>
<td>89.7</td>
<td>92.8</td>
</tr>
</tbody>
</table>

Modifiable Factors with Achievement of Optimal Convective Dose in Postdilution HDF

4176 sessions - 366 patients on postdilution HDF
1-month observational cohort study

Vascular Access Type and Achievement of Optimal Convective Dose in Postdilution HDF

Hematocrit & Albumin and Achievement of Optimal Convective Dose in Postdilution HDF

Mode of Substitution Matters

Post-Dilution HDF: reference

Manual versus Automated Delivery
- Manual Management
- Ultrafiltration Control
Substitution Flow and TMP Profiles
HF80 filter and Manual Post-HDF

HF80S, Manual Post-HDF

Innovative Technology & Intelligent HDF Machine Facilitate Achievement of High Convective Volume

Continuous analysis of hemorheological conditions

UF constant

Continuous adaptation of ultrafiltration flow

Ultrafiltration control by AutoSubplus with FX CorDiax
Substitution Flow and TMP Profiles
Post-HDF Manual vs Pre-HDF AutoSub

Substitution Flow and TMP Profiles
Post-HDF Manual vs Post-HDF AutoSub Plus
Substitution Flow and TMP Profiles
Post-HDF Manual vs Pre-HDF AutoSub Plus
Automatic Control of Ultrafiltration by AutoSub Plus Increases Filtration Fraction and Convective Volume

Mode of Substitution Matters

Mixed-Dilution HDF: as alternative

Automated Delivery

- TMP Control
- Substitution Adjustment
- Ultrafiltration Control
Mixed-Dilution Hemodiafiltration
Original Setting During Clinical Trial

Mixed-Dilution Hemodiafiltration

Typical Behavior of Substitution Flow (post/pre) in Mixed-HDF

Protein Cake Formation onto the Membrane
Protein Gel Layer Formation During Convective Therapy

1. Blood Flow
2. Ultrafiltration
3. Hematocrit
4. Protein concentration

Blood Flow

Fluid Boundary Layer

\[ J_f C_{p(bulk)} \]

Protein Flux Toward Membrane

Average Protein Concentration \( \overline{C}_{p(bulk)} \)

\[ K (C_{p(wall)} - \overline{C}_{p(bulk)}) \]

Protein Flux Away From Membrane

Ultrafiltration Membrane

UFR
Protein Gel Layer Formation
Hemodialysis, Postdilution vs Mixeddilution HDF

Pressure Regime
Hemodialysis

Qb 400-400
TMP 100
Blood Flow

Pressure Regime
Postdilution HDF

Qb 400-300
TMP 300
Blood Flow

Pressure Regime
Mixed or Pre-dilution HDF

Qb 600-400
TMP 200
Blood Flow
Ultrafiltration Flow & Protein Gel Layer Formation Reduces Solutes Sieving Coefficient

Henderson LW et al, ASAIO
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Mixed-Dilution HDF Machine vs Standard HDF

5008 Mixed HDF

5008 & 5008S HDF Post or Pre-HDF
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Mixed-Dilution HDF Machine vs Standard HDF

5008 Mixed HDF

Predilution Pump
Blood Pump
Postdilution Pump
Substitution Port

5008 & 5008S HDF Post or Pre-HDF

Unipuncture Blood Pump
Blood Pump
Substitution Port
Plasma Water and Water Flow Rates

Plasma Water Fraction = \((1 - H) \times (1 - PT)\)

Plasma Water Fraction = \((1 - 0,33) \times (1 - 0,07) = 0,62\)

Plasma Water Flow = \(Q_B \times \text{Plasma Water Fraction}\)

Plasma Water Flow = \(400 \times 0.62 = 248 \text{ ml/min}\)
Mixed-Dilution HDF Machine
Prescription & Monitoring Screen

- Mode HDF
- Auto-Sub
- I/O
- Expected Substitution Volume
- Cumulative Substitution Volume
- Nom HDF Filter (no impact on loop)
- Effective TMP
- Hematocrit
- Trans Membrane Ratio
  Total Substitution Flow/Qb, (%Qb)
- Effective Qb
- Pre Substitution Flow
- Post Substitution Flow
- Automated Adaptation I/O
- Filtration Ratio
  Postdilution Subs. Flow/Qb, (% Qb)
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HDF Predilution vs Mixeddilution with Low Blood Flow

38 ESKD patients – 6 centers

Low blood flow ≤300ml/min

Cross-Over RCT

HDF pre Qb250
HDF pre Qb350
HDF mixed Qb250
HDF mixed Qb300

FX1000HDF

eKt/v, PR-P, PR-B2M, PR-Myogl. Albumin Lost

Albumin Lost per Session

eKt/V

Percent Reduction of B2-Microglobulin

### Substitution Volumes Achieved in the Different Modalities

<table>
<thead>
<tr>
<th></th>
<th>PRE250</th>
<th>PRE300</th>
<th>MIX250</th>
<th>MIX300</th>
</tr>
</thead>
<tbody>
<tr>
<td>UF/4 h, ml</td>
<td>2,463±576</td>
<td>2,449±641</td>
<td>2,436±774</td>
<td>2,377±736</td>
</tr>
<tr>
<td>PBV, l</td>
<td>57.3±1.9</td>
<td>68.5±2.5</td>
<td>57.4±1.8</td>
<td>67.6±3.3</td>
</tr>
<tr>
<td>VS$_{total}$, l</td>
<td>36.5±7.6</td>
<td>41.3±10.9</td>
<td>23.8±1.9</td>
<td>28.5±2.4</td>
</tr>
<tr>
<td>VS$_{pre}$, l</td>
<td>36.5±7.6</td>
<td>41.3±10.9</td>
<td>7.0±0.7</td>
<td>10.1±3.0</td>
</tr>
<tr>
<td>VS$_{post}$, l</td>
<td>36.5±7.6</td>
<td>41.3±10.9</td>
<td>16.8±1.7</td>
<td>18.4±2.8</td>
</tr>
<tr>
<td>VS Post eq., l</td>
<td>18.2±3.8</td>
<td>20.7±5.5</td>
<td>27.3±2.3</td>
<td>33.5±3.9</td>
</tr>
</tbody>
</table>

PBV, processed blood volume  
UF, weight loss  
VS total, total ultrafiltration per session  
VS pre, ultrafiltration in predilution  
VS post, ultrafiltration in postdilution
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β2-Microglobuline Removal Post vs Mixed-HDF with Different Regimes

Direct dialysis quantification by dialysate collection

Performances Comparison Post vs Mixed-HDF

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Hemodialysis</th>
<th>Post-hemodiafiltration</th>
<th>Mixed hemodiafiltration</th>
</tr>
</thead>
<tbody>
<tr>
<td>$Q_{PWm}$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Start</td>
<td>227 ± 35</td>
<td>231 ± 34</td>
<td>230 ± 35</td>
</tr>
<tr>
<td>End</td>
<td>210 ± 32</td>
<td>212 ± 31</td>
<td>212 ± 33</td>
</tr>
<tr>
<td>$Q_{Sprc-D}$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Start</td>
<td>—</td>
<td>—</td>
<td>65 ± 28</td>
</tr>
<tr>
<td>End</td>
<td>—</td>
<td>—</td>
<td>98 ± 41</td>
</tr>
<tr>
<td>$Q_{Sprs-D}$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Start</td>
<td>—</td>
<td>145 ± 20</td>
<td>122 ± 18</td>
</tr>
<tr>
<td>End</td>
<td>—</td>
<td>124 ± 22</td>
<td>90 ± 20</td>
</tr>
<tr>
<td>FF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Start</td>
<td>—</td>
<td>0.67 ± 0.05</td>
<td>0.67 ± 0.06</td>
</tr>
<tr>
<td>End</td>
<td>—</td>
<td>0.64 ± 0.07</td>
<td>0.64 ± 0.05</td>
</tr>
</tbody>
</table>

Transmembrane Pressure Behavior According to HDF Modalities

Transmembrane Modulation to Optimize Performances and Reduce Albumin Loss

Constant TMP at around 300mmHg

Profiled TMP

Pedrini L et al, Kidney Int. 2006;69:573-579
## Albumin Loss at the Start and the End of HDF with Different Procedures

<table>
<thead>
<tr>
<th></th>
<th>Constant TMP N=12</th>
<th>Profiled TMP N=12</th>
<th>P-value(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mass in dialysate (g)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Start – 30 min</td>
<td>0.98 ± 0.18</td>
<td>0.62 ± 0.14</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>30 min – end</td>
<td>4.26 ± 0.78</td>
<td>3.36 ± 1.15</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Total</td>
<td>5.24 ± 0.77</td>
<td>3.98 ± 1.19</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Rate of loss (mg/min)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Start – 30 min</td>
<td>32.6 ± 6.0</td>
<td>20.6 ± 4.7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>30 min – end</td>
<td>22.7 ± 2.7(^b)</td>
<td>17.8 ± 5.5</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Total</td>
<td>24.1 ± 2.1</td>
<td>18.2 ± 4.9</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

\(^a\) P-values calculated using a paired t-test.

\(^b\) Significant difference between start and end values.
Instantaneous β2-M Clearance at the Start and the End of HDF

Pedrini L et al, Kidney Int. 2006;69:573-579
Behavior of Ultrafiltration Coefficient (KUF)

**HF80S**

**FX100**

\[ K_{UF} = \frac{Q_{UF}}{TMP} \]

- **a. Constant TMP**
- **b. Profiled TMP**

Pilot Study

- Prospective open randomized study
- 6 stable anuric ESKD patients on regular RRT
- Treatment schedule 3 x 240 min per week
- All AVF – Needles 15 gauges
- Cordiax HDF5008, FMC
- Qb = 350 ml/min - Qd = 600 ml/min - Qsub = AutoSub

Study protocol
  Each patient explored over two sessions one week apart: HD vs HDF
  - 2 pat **HD** Cordiax100 - **HFD POST** Cordiax1000 (AS)
  - 2 pat **HD** Cordiax100 - **HFD PRE** Cordiax1000 (AS)
  - 2 pat **HD** Cordiax100 - **HFD MIXED** Cordiax1000 (Auto)

- Pre and post dialysis blood samples
- Percent reduction of selected solutes normalized for hemoconcentration

*Approved by Medical Ethical Committee of CH Caen

Courtesy Dr J Potier, Cherbourg
## Characteristics of FX Dialyzers

<table>
<thead>
<tr>
<th></th>
<th>FX100</th>
<th>Cordiax 100</th>
<th>FX1000</th>
<th>Cordiax 1000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Membrane material</td>
<td>Helixone</td>
<td>Helixone plus</td>
<td>Helixone</td>
<td>Helixone plus</td>
</tr>
<tr>
<td>Surface Area, m²</td>
<td>2.2</td>
<td>2.2</td>
<td>2.2</td>
<td>2.3</td>
</tr>
<tr>
<td>KoA Urea, ml/min</td>
<td>1354</td>
<td>1545</td>
<td><strong>1354</strong></td>
<td><strong>1421</strong></td>
</tr>
<tr>
<td>Diameter, μm</td>
<td>185</td>
<td>185</td>
<td>210</td>
<td>210</td>
</tr>
<tr>
<td>Kuf, ml/h/mmHg</td>
<td>73</td>
<td>68</td>
<td>75</td>
<td>76</td>
</tr>
<tr>
<td>SC-β2M</td>
<td>0.8</td>
<td><strong>0.9</strong></td>
<td>0.8</td>
<td><strong>0.9</strong></td>
</tr>
<tr>
<td>SC-Myog</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>SC-Alb</td>
<td>0.001</td>
<td>&lt;0.001</td>
<td>0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Courtesy Dr J Potier, Cherbourg
Dialysis duration 240 min

Substitution flow prescription
- **QSub Pre** = Qsub Post x 2
- **Qsub Mixed** = QSub Post x 1.4

Blood flow, QB (ml/min)
Volume Blood Processed, VBP (l/SES)
Substitution Flow, QSub (ml/min)
Volume Substituted, VS (l/SES)

QBP 350 ml/min

![Graph showing values for Blood flow, VBP, and Qsub]

38.2 ±2.5
26.9 ±0.6
52.0 ±0.6

Courtesy Dr J Potier, Cherbourg
β2-Microglobulin, 12.8Kda

PR β2M, %

\[
\begin{align*}
\text{74.3} & \pm 3.3 \\
\text{83.8} & \pm 2.6 \\
\text{84.3} & \pm 0.1 \\
\text{82.2} & \pm 3.4
\end{align*}
\]

Nephelometry

\[N < 2.4 \text{mg/L}\]
\[X \pm SD 28.3 \pm 5.4\]

Courtesy Dr J Potier, Cherbourg
TNF α, 17-50 KDa

PR TNF-a, %

58.6 ± 7.0
65.5 ± 1.3
57.3 ± 10.6
62.6 ± 3.0

Elisa R&D
N: < 1.9 pg/mL
X ± SD: 12.3 ± 3.2 (8.8 to 19.4)

Courtesy Dr J Potier, Cherbourg
Myoglobin, 17.2KDa

Nephelometry
N : 24-72 ng/mL
X±SD: 199 ±79 (88 à 345)

Courtesy Dr J Potier, Cherbourg
Prolactin, 23.0 KDa

ELISA Biomerieux

N M 2 à 15 – F 3-20 ng/mL
X±SD 29.5 ±25.3 (9.2 à 84.1)

PR Prol, %

<table>
<thead>
<tr>
<th></th>
<th>54.7 ±8.3</th>
<th>79.2 ±6.7</th>
<th>86.8 ±4.4</th>
<th>64.7 ±7.4</th>
</tr>
</thead>
<tbody>
<tr>
<td>sProl</td>
<td>29.5 ±25.3</td>
<td>23.4 ±11.6</td>
<td>52.8 ±44.3</td>
<td>12.2 ±4.2</td>
</tr>
</tbody>
</table>

Courtesy Dr J Potier, Cherbourg
IL-6, 24.5KDa

PR IL-6, %

<table>
<thead>
<tr>
<th></th>
<th>29.3</th>
<th>12.3</th>
<th>50.2</th>
<th>36.2</th>
</tr>
</thead>
<tbody>
<tr>
<td>±</td>
<td>±0.4</td>
<td>±36.8</td>
<td>±38.6</td>
<td>±12.5</td>
</tr>
</tbody>
</table>

Elisa R&D

N < 2.1 pg/mL
X ± SD: 1.41 ± 0.72 (0.35 à 2.47)

Courtesy Dr J Potier, Cherbourg
Free Light-Chain Kappa, 25.0KDa

Free Lite
N 3.3 à 19.4mg/L
X±SD 122.7 ± 63.1 (25.5 à 229)

Courtesy Dr J Potier, Cherbourg
Free Light Chain Lambda, 50.0KDa

Free Lite
N 5.7 à 26.3 mg/L
X±SD 75.3 ±35.9 (29.4 à 161)

PR FLCL, %

<table>
<thead>
<tr>
<th></th>
<th>HD</th>
<th>HDF MIX</th>
<th>HDF POST</th>
<th>HDF PRE</th>
</tr>
</thead>
<tbody>
<tr>
<td>75.8</td>
<td>75.8</td>
<td>102.3</td>
<td>66.5</td>
<td>55.9</td>
</tr>
<tr>
<td>±23.4</td>
<td>±83.0</td>
<td>±4.7</td>
<td>±37.4</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>±15.6</td>
<td>±10.7</td>
<td>±16.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>±15.6</td>
<td>±10.7</td>
<td>±0.0</td>
</tr>
</tbody>
</table>

Courtesy Dr J Potier, Cherbourg
FGF23, 32.KDa

<table>
<thead>
<tr>
<th>RR%</th>
<th>Value</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>38.7</td>
<td>±7.8</td>
<td></td>
</tr>
<tr>
<td>68.3</td>
<td>±0.5</td>
<td></td>
</tr>
<tr>
<td>67.6</td>
<td>±0.9</td>
<td></td>
</tr>
<tr>
<td>66.3</td>
<td>±11.8</td>
<td></td>
</tr>
</tbody>
</table>

Elisa merck/millipore
N: pg/mL
X±SD 919 ±1558 (52 à 4280)

Courtesy Dr J Potier, Cherbourg
Albumin Loss as Function of QSubstitution

FX1000_{HDF} vs Cordiax1000

 Courtesy Dr J Potier, Cherbourg
Outlook of the Presentation

1. What is optimal in convective therapies?
   - Convective dose: postdilution HDF as reference

2. What's matter in HDF?
   - Dilution mode: Post - Pre - Mixed - Mid

3. Why mixed-HDF is necessary?
   - Medical & engineering rationale

4. How to use mixed-HDF?
   - Technical aspects
   - Nursing & Doctor perspectives

5. What indications?

6. What results?

7. Take home message
Take Home Message

• Benefits of HDF are depending on convective dose delivered
• Postdilution HDF is still the reference method for convective therapies in RRT
• Minimum threshold total ultrafiltered volume to improve better outcome is closed to 40L/m²/wk or 70L/1.73m²
• Automated ultrafiltration control by AutoSubPlus permits to achieve this volume in more than 75% of CKD patients
• Mixed-HDF main facilitate implementation of HDF in the remaining 25% of CKD patients with hemorheologic unfavorable profile
• Poor blood flow, catheters, elderly and kids may benefit from mixed-HDF
• Long-term studies are still missing to define specific indications and benefits