Not Too fast, Not Too Slow: Striking the Optimal Balance in Hemodialysis Fluid Management

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Outline

- Fluid management: the conundrum
- Ultrafiltration rate and outcomes
- Extracellular volume overload and outcomes
- Clinical cases and management strategies
Fluid management: the conundrum
Call for “Volume First” Approach

“Good fluid management” identified as “one of the most essential unmet needs of the contemporary dialysis population.”

| Extracellular volume | Fluid removal rate | Interdialytic weight gain |
Hemodynamic instability
• End-organ ischemia
• Patient discomfort

Hypovolemia

Overly rapid ultrafiltration rate

Hypertension
• Ventricular hypertrophy
• Heart failure, arrhythmia
• Patient discomfort

Overly slow ultrafiltration rate

Hypervolemia
Hypovolemia

Overly rapid ultrafiltration rate

Overly slow ultrafiltration rate

Hypervolemia
They said [cramps] are close to what a man feels like having a baby. If that's the way it is, boy, I wouldn’t want to have one. [60y M]

As soon as the cramps start, I’m yelling’. You never die, but it's so painful that you think that you do. [55y F]

It feels terrible because sometimes I'll be gasping for breath. I start crying because I can't breathe. It's like my own lungs is shutting down and I just can't get the breath that I need. [49y F]

I just kind of panic when I can’t get a deep breath. It’s like I feel like I’m going to smother. [76y F]

Ultrafiltration rate and outcomes
Ultrafiltration rate

\[
\text{UF rate (mL/h/kg)} = \frac{\text{IDWG (mL)}}{\text{TT (h)}} / \text{Post-weight (kg)}
\]

UF = ultrafiltration

IDWG = interdialytic weight gain

TT = treatment time (dialysis session length)
Higher UF rate → death

Higher UF rate $\rightarrow$ death

- U.S. cohort (N=118,394)

<table>
<thead>
<tr>
<th>UF rate (mL/h/kg)</th>
<th>All-cause mortality</th>
<th>Adjusted HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;10 (vs. ≤10)</td>
<td></td>
<td>1.22 (1.20-1.24)</td>
</tr>
<tr>
<td>&gt;13 (vs. ≤13)</td>
<td></td>
<td>1.31 (1.28-1.34)</td>
</tr>
</tbody>
</table>

- Consistent across sex, race, ethnicity, vintage, and treatment time
- Consistent when considered relative to weight (kg), BMI (kg/m$^2$), and BSA (m$^2$)

Higher UF rate → death

- U.S. cohort (N=118,394)

<table>
<thead>
<tr>
<th>UF rate (mL/h/kg)</th>
<th>All-cause mortality Adjusted HR (95% CI)</th>
</tr>
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<tbody>
<tr>
<td>&lt;6</td>
<td>1.00 (reference)</td>
</tr>
<tr>
<td>6-8</td>
<td>1.03 (1.00-1.07)</td>
</tr>
<tr>
<td>8-10</td>
<td>1.09 (1.06-1.12)</td>
</tr>
<tr>
<td>10-12</td>
<td>1.15 (1.12-1.19)</td>
</tr>
<tr>
<td>12-14</td>
<td>1.22 (1.18-1.27)</td>
</tr>
<tr>
<td>&gt;14</td>
<td>1.43 (1.39-1.48)</td>
</tr>
</tbody>
</table>

Higher UF rate $\rightarrow$ longer recovery time

- U.S. cohort (N=2,689)
UF rate > plasma refill rate \( \Rightarrow \) hypotension
Intradialytic hypotension (IDH) → death

- N=39,497 incident HD patients (U.S.)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>(+) IDH in &gt;10% tmts</th>
<th>Adjusted HR (95% CI)</th>
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</thead>
<tbody>
<tr>
<td>All-cause mortality</td>
<td>1.19 (1.06 – 1.34)</td>
<td></td>
</tr>
<tr>
<td>Cardiovascular (CV) mortality</td>
<td>1.22 (1.02 – 1.48)</td>
<td></td>
</tr>
<tr>
<td>Fluid overload hospitalization</td>
<td>1.22 (1.11 – 1.34)</td>
<td></td>
</tr>
<tr>
<td>Major CV event</td>
<td>1.29 (1.19 – 1.40)</td>
<td></td>
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</tbody>
</table>

Intradialytic hypotension (IDH) → death

- IDH: Nadir systolic BP < 90 mmHg in > 30% of treatments
- Prevalent HD patients

<table>
<thead>
<tr>
<th>IDH (vs. no IDH)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dialysis Org. Cohort (N=10,392)</td>
<td>1.30 (1.07 – 1.57)</td>
</tr>
<tr>
<td>HEMO Study cohort (N=1,753)</td>
<td>1.38 (1.11 – 1.71)</td>
</tr>
</tbody>
</table>

Hypotension
Hypervolemia
Cardiac Structural Change
Myocardial Stunning
↑ Ultrafiltration Rate
↓ Treatment Time
↑ Weight Gain
↑ Morbidity and Mortality

Hypo-perfusion of other vascular beds
Procedural modifications
Myocardial Stunning
Hypervolemia
Cardiac Structural Change

UF rate $\rightarrow$ IDH $\leftrightarrow$ cardiac stunning $\rightarrow$ death

Higher UF rate $\rightarrow$ other organ stunning $\rightarrow$ death

Clinical Quality Indicator

Average UF rate $>13$ mL/h/kg
U.S. threshold: 10.1%

UF Rate Measure

% of patients in the facility with average UF rate $\geq 13$ mL/h/kg
UF rate (mL/h/kg) = \frac{IDWG (mL)}{TT (h)} / Post-weight (kg)

UF = ultrafiltration
IDWG = interdialytic weight gain
TT = treatment time
Treatment time: patient preferences

- 15m TT extension: 44.6% 
- 30m TT extension: 21.3% 
- 45m TT extension: 9.7% 
- 4th treatment: 12.2%

Treatment time: clinic operational burden

IDWG reduction via fluid restriction

- Fluid restrictions: poor adherence:
  - Surveyed 437 patients with fluid restrictions
  - >40% adhered to prescribed fluid restriction <1 day/ week

- Virtually impossible (and inhumane) in over-salted individuals

Extracellular volume overload and outcomes
Goal = extracellular euvolemia

Incorrect target weight (i.e. wrong “dry” weight)

Failure to achieve target weight
Target weight estimation in practice

Tools
- Blood volume monitor
- Bioimpedance
- Biomarkers
Extracellular volume overload (BVM) $\rightarrow$ death

- U.S. cohort (N=308)
Extracellular volume overload $\rightarrow$ death

- 26 country cohort
- Volume status by multi-frequency bioimpedance

Baseline fluid overload
$N=39,566$

1-year cumulative fluid overload
$N=22,845$

Post-dialysis weight > target weight $\rightarrow$ death

- Italian cohort (N=182)
Post-dialysis weight > target weight → 30-day death

- U.S. cohort (N=113,561)

Extracellular volume overload $\rightarrow$ fatigue

- 110 hemodialysis patients with multi-frequency biompedance

<table>
<thead>
<tr>
<th>Multivariable linear regression model (adjusted $R^2=0.41$)</th>
<th>Multi-dimensional fatigue inventory score $\beta$ (p-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beck Depression Inventory</td>
<td>20.8 (&lt;0.001)</td>
</tr>
<tr>
<td>Recovery time $&gt;$8h</td>
<td>11.4 (0.001)</td>
</tr>
<tr>
<td>Post-HD %ECW/TBW</td>
<td>2.9 (0.002)</td>
</tr>
<tr>
<td>Muscle wasting</td>
<td>-5.7 (0.05)</td>
</tr>
</tbody>
</table>

UF rate minimization without volume expansion
Fluid management cases
Clinical Case 1

• 55y man
  • Diabetes, heart failure (EF 45%, history of hospitalizations)
  • Myasthenia gravis on bimonthly plasmapheresis

• Hemodialysis
  • IDWG = 3 - 4.5 kg
  • TT = 3.5 hours T-R-Sat
  • Target weight = 73 kg
  • Post-weights = ~73 kg
  • Anuric
  • Mean pre-HD systolic BP 110s
  • eKt/V = 1.6

UF rate = 11.7 – 17.6 mL/h/kg

Weekly mean
UF rate = 14.6 mL/h/kg

Asymptomatic hypotension
13 (mL/h/kg)
UF rate

= \frac{IDWG \; (kg)}{TT \; (h)}

\div

73 \; (kg)
Post-weight
**Tuesday**

- 4 h treatment
- weekend IDWG goal = <3.8 kg
- 1.3 L/day w 72 h break
- ~13 mL/h/kg

**Thursday and Saturday**

- 3.25 h treatment
- IDWG goal = <3 kg
- 1.5 L/day w 48 h break
- ~12.6 mL/h/kg

- 10.5 h/week treatment
- Actual mean UF rate = 12 mL/h/kg
Strategies

- Case 1: Longer treatments after the long interdialytic break
Clinical Case 2

• 49y man with hypertension

• Hemodialysis
  • Typical IDWG = 1 – 2 kg
  • TT = 3h M-W-F
  • Target weight = 51.5 kg
  • But… one Monday, IDWG: 4 kg

UF rate = 6.5 - 12.9 mL/h/kg

UF rate = 25.9 mL/h/kg
Take the long view

<table>
<thead>
<tr>
<th>Sun</th>
<th>Mon</th>
<th>Tues</th>
<th>Wed</th>
<th>Thurs</th>
<th>Fri</th>
<th>Sat</th>
</tr>
</thead>
</table>

Goal: target weight achievement by the end of the week
Case: Finding the balance

<table>
<thead>
<tr>
<th></th>
<th>Monday</th>
<th>Wednesday</th>
<th>Friday</th>
</tr>
</thead>
<tbody>
<tr>
<td>TT</td>
<td>3 h</td>
<td>3 h</td>
<td>3 h</td>
</tr>
<tr>
<td>Target wt</td>
<td>51.5 kg</td>
<td>51.5 kg</td>
<td>51.5 kg</td>
</tr>
<tr>
<td>IDWG</td>
<td>4 kg</td>
<td>1 kg</td>
<td>1 kg</td>
</tr>
<tr>
<td>Pre-wt</td>
<td>55.5</td>
<td>54 kg</td>
<td>53 kg</td>
</tr>
<tr>
<td>UF volume</td>
<td>2.5 L</td>
<td>2 L</td>
<td>1.5 L</td>
</tr>
<tr>
<td>UF rate</td>
<td>16.2 mL/h/kg</td>
<td>12.9 mL/h/kg</td>
<td>9.7 mL/h/kg</td>
</tr>
<tr>
<td>Post-wt</td>
<td>53 kg</td>
<td>52 kg</td>
<td>51.5 kg</td>
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Success contingent on controlled IDWG for remainder of week
Strategies

- Case 1: Longer treatments after the long interdialytic break
- Case 2: Balance UF rate and fluid overload-related harms
Clinical Case 3

- 48y woman with vascular disease s/p L BKA, heart failure (EF 40%)

Hemodialysis
- Typical IDWG = 2.5 – 3 kg
- TT = 3.5h T-R-Sat
- Target weight = 82.0 kg

- Pre-HD SBP: 90s (nadir ~80 mmHg)
- Leg cramping ¾ way through treatment

UF rate = 8.7 - 10.4 mL/h/kg

Hypotension

Cramping
Identify and align goals

Medical Goals
- Minimize cardiovascular risk
- Avoid hypotension
- Prevent cramping

Patient Goals
- Spend time with family
- Pain-free dialysis
  - Cramping
  - Post-dialysis fatigue

Goal-directed Dialysis
- ↑ TT to 4 hours for 4 weeks
- Follow symptoms weekly (cramping, recovery time)
- (+) Patient-perceived improvement: maintain TT ↑
- (-) Patient-perceived improvement: return to prior TT
Strategies

- Case 1: Longer treatments after the long interdialytic break
- Case 2: Balance UF rate and fluid overload-related harms
- Case 3: Time-limited, symptom-guided trials (connect to patient goals)
Clinical Case 4

- 66y man with heart failure (EF 25%) with frequent hospitalizations

- Hemodialysis
  - Typical IDWG = 3 – 3.5 kg
  - TT = 4h M-W-F
  - Target weight = 70 kg
  - Post-HD weights (last 4 treatments)
    - Mon: 73 kg
    - Wed: 72 kg
    - Fri: 71.5 kg
    - Mon: 72 kg

UF rate = 10.7 - 12.5 mL/h/kg

Failure to achieve target wt
Target weight prescription and readmissions

- \( N = 44,460 \) patients with hospitalizations
- Exposure: target weight adjustment (vs. not) within 7 days of hospital discharge

<table>
<thead>
<tr>
<th># needed to treat</th>
<th>ED visit*</th>
<th>Readmission*</th>
<th>Composite outcome*</th>
</tr>
</thead>
<tbody>
<tr>
<td>114</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>61</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>49</td>
<td></td>
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*30-day outcomes

Target weight achievement vigilance

• Identify target weight achievement problem
  • Assess reasons (hemodynamics, symptoms, other)
  • Target weight adjustment? (exam, history, treatment tolerance and history)
  • Additional treatment?
  • Treatment time adjustment?
  • Other

• Take action
  • Root cause: single episode of large IDWG 10 days ago
  • Solution: add single extra treatment (2h) to return to target weight
Strategies

- Case 1: Longer treatments after the long interdialytic break
- Case 2: Balance UF rate and fluid overload-related harms
- Case 3: Time-limited, symptom guided trials
- Case 4: Target weight achievement vigilance and extra treatment
Clinical practice suggestions

• Case 1: Longer treatments after the long interdialytic break
• Case 2: Balance UF rate and fluid overload-related harms
• Case 3: Time-limited, symptom guided trials
• Case 4: Target weight achievement vigilance and extra treatment

• Lower interdialytic weight gain through a focus on sodium
• In-center nocturnal hemodialysis
• Send patients home
• Ultrafiltration profiling?

Strategy must be individualized and take into account patient preferences and treatment goals
Summary

• Higher UF rates are associated with adverse outcomes.

• Extracellular volume expansion is associated with adverse outcomes.

• Euvolemia achievement and UF rate minimization are both important. Their relative importance is unknown.

• Fluid management plans should be individualized based on patient risk profiles, preferences and, possibly, symptoms.
Feedback requested: Research Readiness Toolkit

1. WATCH → video
2. REVIEW → materials
3. TALK → discussion questions
4. RECORD → research preferences

Discussion Guide

Video

Written Materials

Lunch & Learn Module

Julia Narendra
UNC Dialysis Research Team
Questions?