Hypotension
extracorporeal circuits
Determinants of renal recovery

Augustine et al AmJKidDis 2004

Urine output
% day 3/day 1
Urine output
day 1 /ml
ΔMAP on
dialysis

Case Western
Univ Hospitals
Cleveland
80 AKI pts
95% CL
* p < 0.05

0 1 2 3 4 5
odds ratio
Renal autoregulation


Renal blood flow ml/min

control

3 weeks

1 week

rat model
time from ischemic insult

mean arterial pressure mmHg

90 100 110 120
Renal autoregulation

Redfors et al IntensivCareMed 2011

MAP mmHg

GFR ml/min

Post CBS
Intradialytic hypotension

KDOQI
ERA Best Practice Guidelines

\[ \downarrow \text{SBP} \geq 20 \text{ mmHg or } \downarrow \text{MAP} \geq 20 \text{ mmHg} \]
associated with clinical events requiring intervention
Deterioration during CRRT

- deterioration within 10 minutes
- hypotensive
- hypoxia
  - cardiac arrest
Hypotension

No anticoagulant

120 ml/min

No UF

Dialysate

Replacement fluid

straight swap connection
1968 Bioincompatibility = Leukopenia

Kaplow LS, Goffinet JA.
Profound neutropenia during the early phase of hemodialysis.
*JAMA* 1968; 203: 1135-7

Toren M, Goffinet JA Kaplow LS.
Pulmonary bed sequestration of neutrophils during the early phase of hemodialysis.
*Blood* 1970; 36: 337-40
Contact activation

Vroman et al. Blood 1980

Blood flow

Boundary layer

Dialyzer membrane

Vroman effect
Bradykinin

Stoves et al. ArtifOrgans 2001
Membrane interactions - bradykinin

Hackbarth et al Pediatr Nephrol 2005

In vitro circuit
PAN69

[Graph showing bradykinin levels over time for CVVH, CVVHD, CVVD, and CVVH]
Bradykinin – Nitric oxide

Coppo et al KidInt 2000
Bradykinin - Nitric oxide

Coppo et al KidInt 2000
Question

What priming fluid to use?
isotonic bicarbonate
Bradykinin

Coppo et al KidInt 2000

The diagram shows the levels of bradykinin fmol/l for different groups: AN69, AN69SPANDX, PS, CTA, and CU. The graph indicates varying levels of bradykinin across these groups, with some showing higher levels compared to others.
Nitric Oxide

Coppo et al KidInt 2000

[Bar graph showing NOS activity (pmol/min/mg) for different conditions: AN69, AN69S/PANDX, PS, CTA, and CU. The graph indicates varying levels of NOS activity across the conditions.]
Question

What dialyzer to use?

Cu
HM
PA
PS
CTA
PAN69
What dialyzer to use?

Your choice

A

V
Bradykinin

Stoves et al ArtifOrgans 2001

Bradykinin pg/ml

CVVHDF

CVVHD

300

200

100

0
Question

What dialysis modality to start?

- dialysis
- filtration
- straight swap connection
Answer

dialysis

straight swap connection
Question

What blood pump speed to start?
Low $Q_b$ protocol

Baldwin et al

**MAP**

- Baseline: 205
- ≤10%: 530
- 11-20%: 184
- > 20% UP: 67
- > 20% DOWN: 26

**NAdr**

- Baseline: 205
- ≤10%: 338
- 11-20%: 167
- > 20% UP: 145
- > 20% DOWN: 157

Pts MAP < 50

$Q_b$ 50 ml/min $\uparrow$ by 20-50 ml/min
No grade A evidence
But slow would seem appropriate

Answer
dialysis

straight swap connection

50-100 ml/min
Bradykinin

Bradykinin pg/ml

PAN 69

PS
Bradykinin pg/ml
Plasma aminopeptidase - phenotypes

Chanard et al KidInt 2006

![Graph showing APP activity (pmol/min/ml) for yes, no hypersensitivity and reference. The graph indicates that the APP activity is significantly higher in the reference group compared to the no hypersensitivity group, with a non-significant difference between yes and no hypersensitivity groups.](Image)
Nitric Oxide

Nitric Oxide nmol/l

controls  systemic sepsis  ALF

UCL
Membrane interactions

Mares et al KI 2009

polysulphone dialyzer
Lectin - Toll R activation
Membrane interactions - platelets

Ballota et al JThoracicSurg 2007
Membranes designed for absorption

Univ Lyon
Pig model
Enotoxic shock
Mean (SD)

Rimmele et al Nephrol Dial Transplant 2009
Hypotension

Anticoagulant

120 ml/min
Heparin

Repeat unit of heparin
Heparin reactions

Pre formed Ab to porcine Ag

Ab to Heprin-PF4

charge reactions
Heparin reactions

Contact coagulation pathway

C3a ← C3
C5a ← C5
bradykinin ← HMWt kininogen
plasma kallikrein

-vely charged membrane

XII

plasma prekallikrein

XIIa

XII

XI

XIa
Anticoagulants and bradykinin generation

Kanke et al BloodPurif 2007

Log Bradykinin pg/ml

DOKKYO Med Univ Mibu, Japan Cellsorba EX Membrane 10 pts

Pre membrane Post membrane

Nafamostat Maleate 20 mg/h
UFH 3000 IU/h
NM 1 mg/h + LWMH 1000 IU/h
LWMH 1-3000 IU/h
heparin administration
Answer

venous heparin administration
Sudden collapse on dialysis

80 year old man
recently switched from PD to HD following peritonitis
due for discharge home after dialysis today

- Patient felt dizzy < 5 min starting dialysis
- sudden hypotension
  - BP unrecordable
  - PaO2 2.24 kPa PaCO2 6.34 kPA
- unconscious
- cardiac arrest
HD sessions

Peripheral platelet count x 10^12/l

Pre- post admission

Time days
dense granule containing ADP

\( \text{FcgIIa receptor} \)

heparin binding site

\( \alpha \) granule containing PF4

HIT-Ab

activates endothelium

heparin-PF4 complex conformational change

free heparin

endothelial cell

heparan sulphate

HIT-Ab binds to platelets

releases micro-particles (tissue factor)
Pseudo-pulmonary embolism

acute alveolar shaddowing due to interstitial lung edema secondary to HIT
## Pre-test probability

<table>
<thead>
<tr>
<th>score</th>
<th>3</th>
<th>1</th>
<th>0</th>
</tr>
</thead>
<tbody>
<tr>
<td>↓ Platelets x 10^{12}/l</td>
<td>20-100 or &gt; 50% fall</td>
<td>10-19 or 30-50% fall</td>
<td>&lt; 10 or &lt;30% fall</td>
</tr>
<tr>
<td>Timing of fall plts</td>
<td>5-10 days Heparin</td>
<td>&gt;10 days or timing not clear</td>
<td>&lt; 1 day</td>
</tr>
<tr>
<td>Clinical symptoms</td>
<td>thrombosis acute systemic reaction skin necrosis</td>
<td>progressive recurrent silent thrombosis</td>
<td>none</td>
</tr>
<tr>
<td>Other cause</td>
<td>none evident</td>
<td>possible</td>
<td>definite</td>
</tr>
</tbody>
</table>
Management of HIT type 2
Cardiac perfusion

Chesterton LJ et al Hemodial Int 2009
Hothi MD thesis UCL 2009
Changes in ICP with HVHF
Change in ICP with falling MAP

Time min

ICP

ABP

SJO

\( \text{ABP}_{\text{mmHg}} \)

\( \text{ICP}_{\text{mmHg}} \)

\( \text{SJO}_{2\%} \)
Transcranial Döppler

Mean Blood flow velocity
MCA cm/s

% Δ BFV during HD and UF volume
$r = -0.486$, $p < 0.01$

Stefanidis et al ClinNephrol 2006
**How much UF is needed?**

**Nutrition**
- 30 kcal/kg.day
- 75 kg = 2250 kcal

**RRT modality**
- **CVVH/CVVHDF**
  - Intermittent
  - 3 x 4 h
  - 5 x 4 h
  - 7 x 4 h
  - 7 x 8 h

**UF rate required**
- **anuric patient**
  - 2400 ml/day
  - 100 ml/h
  - 5600 ml/HD
  - 1400 ml/h
  - 3360 ml/HD
  - 840 ml/h
  - 2400 ml/HD
  - 600 ml/h
  - 300 ml/h

**Other**
- 1000 ml αα10%
- 750 ml glucose 40%
- 350 ml lipid 20%

**iv meds infusions**
- Around 3 l/day
The unphysiology of hemodialysis

![Graph showing serum urea levels over a week.]

- **Serum urea mmol/l**

  - Monday (M)
  - Tuesday (T)
  - Wednesday (W)
  - Thursday (Th)
  - Friday (F)
  - Saturday (Sa)
  - Sunday (Su)

- **TAD**
More frequent hemodialysis

Serum urea mmol/l

M | T | W | Th | F | Sa | Su
UF and ↓ BP during HD

Ronco et al Nephrol Dial Transplant 1990

St Orsola Vincenza
HD pts
effect of UF rate
* p < 0.05
RRT for AKI stage 3

CRRT
CVVH
CVVHD
CVVHDF

Peritoneal Dialysis

PIRRT
HYBRID
SEDD
Genius

intermittent
HD
HF
HDF
Genius
CVVH vs intermittent HD

Change in Systolic BP mmHg

baseline 0.5 2 4 24

Univ Frankfurt
Univ Erlangen
Nürnberg

30 pts septic shock AKI
PS /heparin

Q_b 250 ml/min
mean (SD)

* p < 0.05

CVVHF
2 l/h lac

4 h HD bic
UF 0.25-0.5 l/h

John et al NephrolDialTransplant 2001

CVVH vs intermittent HD

John et al NephrolDialTransplant 2001
Daily dialysis for AKI

Schiffl et al NEnglJMed 2002

Univ München
160 AKI pts
80 pts each gp
mean (SD)
*p < 0.05

alt die HD
daily HD

% mortality
days to renal recovery
What ultrafiltration rate?

50 ml/h
100
200
300
400

straight swap connection

70 kg
Hypotension

Refilling

Intravascular Space

Ultrafiltration

Dialyzer

Interstitial Space

UF = 500 to 1000 ml/hr

UF = 50 to 100 ml/hr

No Hypotension
Relative BVM %

duration of hemodialysis hrs

slope of RBV in response to UF

ultrafiltration pulses

S Mitra MD thesis Univ London 2009
Answer

Ultrafiltration rate

Stable outpatient HD risk ≥ 500 ml/h (0.7 ml/kg/h kg)
Dose of RRT for AKI?

Veterans ATN study NEnglJMed 2008

1124 pts AKI

High intensive group
achieved Kt/V >1.2 - 6 x wk
CVVHDF 35 ml/kg.h

Less intensive group
achieved Kt/V >1.2 - 3 x wk
CVVHDF 20 ml/kg.h
### Dialysate Sodium

<table>
<thead>
<tr>
<th>Plus</th>
<th>Minus</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>130</strong></td>
<td>Less weight gain, thirst, and hypertension</td>
</tr>
<tr>
<td><strong>140</strong></td>
<td>Less hypotension on dialysis &amp; post dialysis headache</td>
</tr>
<tr>
<td><strong>140</strong></td>
<td>More weight gain, thirst, and hypertension</td>
</tr>
</tbody>
</table>

**Dialysate sodium**

- More weight gain, thirst, and hypertension
- Less hypertension on dialysis & post dialysis headache
Sodium balance in AKI

Low sodium enteral feeds

- nepro
  - 8.7 mEq/can
  - 3.7 mEq/100 ml

- clinutren
  - 7.0 mEq/carton
  - 3.5 mEq/100 ml

- fresubin
  - 58 mEq/l bag
  - 5.8 mEq/100 ml
Hypotension in pts with AKI

- CRRT
- Haemodialysis

% treatments with ↓BP

French ICU Study Group on AKI Prospective Multicenter Dialysate Na + 10 mmol/l
What dialysate Na to choose?

Dial Na
135
138
141
143
145
148

200 ml/min

straight swap connection
What dialysate Na to choose?

- Dial Na: 143, 145
- Se Na: 138
- 200 ml/min
- Straight swop connection
• dialysate composition
  - Potassium
  - Calcium
  - Magnesium
  - Bicarbonate
  - Glucose
Dialysate [K⁺] and dysrhythmias

High K⁺ reduces QTc Dispersion *Cupista et al.* *Nephron 1999*

“Constant plasma-dialysate K⁺ gradient” of 1.5 mmol/l reduced dysrhythmia *Redaelli et al.* *KI* 1996
## Dialysate [K+]
### Practical Considerations

<table>
<thead>
<tr>
<th>Standard conditions</th>
<th>1-2 mEq/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk of Dysrhythmia</td>
<td>3.0 Meq/l</td>
</tr>
<tr>
<td>Low predialysis [K+]</td>
<td>Individualise</td>
</tr>
<tr>
<td>Acutes</td>
<td></td>
</tr>
</tbody>
</table>
Dialysate glucose

- Previously glucose used as osmotic agent, to generate UF and prevent disequilibrium.
- Currently dialysis glucose concentrations are most commonly zero and 5.5 mmol/l.
- Hypertonic solutions are less often used.
• dialysate Calcium
Hypocalcemia in the ICU

Zivin et al AmJKidDis 2001

Univ Washington Study
199 pts
ionised Ca++< 1.16 mmol/l

ICU patients
ICU but 48 h discharge
hospitalized non ICU
- dialysate calcium
- hypotension
- arrhythmias - QT dispersion
Dialysate Magnesium

- Dialysate Mg 1.0-1.5 mEq/l
- To minimise arrhythmias
- 1.25 – 1.5 mEq/l
dialysate bicarbonate

- alters serum
- potassium, calcium & magnesium

- avoid supra-physiological concentrations
- 28-32 mEq/l
• dialysate temperature
Warm and Cold HD and HF

Thermal effects

DeVries et al JASN 1997  Maastricht

Arterial blood pressure mmHg

UF + HD
cold dialysate

warm HF
cold HF

0       30      60      90     120     150     180

0 30 60 90 120 150 180

75
85
95
105
115
125
135
145

Time (min)
BTM Multicenter Study

Frequency of treatments with hypotensive episodes

E = 0  
T = 0

27 centers
95 hypotensive prone patients
A/B or B/A 4 weeks each.

Hypotension in pts with AKI

French ICU Study Group on AKI Prospective Multicenter Dialysate Na + 10 mmol/l Temp 35°C
Volume management with RRT for AKI

- **Maintenance of fluid balance**
  - Isovolemic patient
  - Isonatraemic balance

- **Avoiding complications**
  - Hypovolaemia
  - Negative sodium balance
  - Hypervolaemia
  - Positive sodium balance
Biofeedback controlled HD - Hemocontrol

- 25%
- 20%
- 15%
- 10%
- 5%
- 0%

Upper tolerance
Actual value
Objective

Lower tolerance
Ideal trajectory

WLR

BV (%)

time (min)

Objective

Ideal trajectory

Upper tolerance

DC

Actual value
FLUID IMBALANCE IN DIALYSIS

Fluid Imbalance

- **Positive**
  - Insufficient fluid removal
  - Fluid Gain
  - Absolute volume (Total UF)

- **Negative**
  - Relative Volume (UF rate)
Machine errors

Most machines do not stop the treatment after multiple overrides of the “fluid balance error” alarm.

However, the some machines force the operator to stop the therapy after a number of repeated alarms.
What are the effects of different RRT modalities on fluid balance?

- IHD: acute loss of plasma volume
  - ultrafiltration rate > refill rate
  - decrease in plasma osmolality and subsequent shift of fluid into extravascular compartments
  - thermal balance
What are the effects of different RRT modalities on fluid balance?

- Convective modalities: better hemodynamic stability
  - more stable plasma osmolality
  - sodium balance
  - cooling effect
- CRRT: cohort and retrospective studies suggest preserved diuresis and greater renal recovery than IHD (grade 4 evidence)
Hemodiafe dialysis

- $[\text{Na}^+]_D \ 10 \text{ mmol/l} > [\text{Na}^+]_P$
- Dialysate Temp 35°C
- Duration – mean time > 5h
Renal support for AKI

**Summary**

- Prevention of hypotension
  - ↑ dialysate Na⁺
  - ↑ IHD time and frequency
  - cooled dialysate
  - ultrapure dialysate
  - bicarbonate dialysate
  - volumetric machine
  - dialyzer
thank you for your attention!