DOUBLE-BLIND RANDOMISED CONTROLLED STUDY OF HIGH CUT-OFF (HCO) POINT VS. STANDARD HEMOFILTRATION IN ACUTE KIDNEY INJURY (ClinicalTrials.gov NCT00912184)

Rafidah Atan[1], Leah Peck[2], John R Prowle[3,4], Glenn Eastwood[2], Rinaldo Bellomo[2]

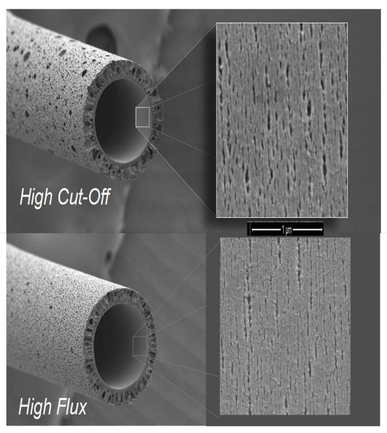
[1]Clinical School Johor Bahru, Monash University Sunway Campus, Malaysia; [2]Department of Intensive Care, Austin Hospital, Victoria, Australia; [3]Barts Health NHS Trust, [4]Queen Mary, University of London

INTRODUCTION

- Severe sepsis and inflammation is associated with the production of cytokines
- Cytokine removal via continuous hemofiltration is a potential adjuvant therapy for shock states
- Conventional hemofilters with cut off point of 30 kD have limited capacity to eliminate cytokines (MW range for cytokines 9 - 50 kD)

High Cut-off Hemofilters

- Higher cut-off point (60kD)
- Potential to improve cytokine clearance
- May also cause inadvertent removal of albumin (66 kD)



- Previous studies have found that HCO hemofiltration offers better cytokine removal and reduced patient noradrenaline requirement compared to standard hemofiltration

OBJECTIVE

To test the hypothesis that HCO hemofiltration offers better cytokine removal and to study its clinical effects

METHODS

- Randomized, double-blind, single-centre, parallel-group controlled study involving 76 adult patients in acute kidney injury (AKI) requiring hemofiltration and on noradrenaline infusion
- Randomized to either HCO or standard hemofiltration (HF)
- Standard settings applied until recovery or 14 days after randomization or death
- Blood and ultrafiltrate sampled for serum cytokines, pro-apoptotic activity and expression of Toll-like receptors on white cells for the first 3 days
- Daily serum albumin levels recorded
- Study filters are indistinguishable

Study filters (HCO vs. standard) are indistinguishable

For each treatment, the following technical settings apply:
- Blood flow at 200 ml/min
- Ultrafiltration rate at 25 ml/kg/min
- Anticoagulation as clinically indicated
- Bicarbonate-buffered replacement fluid

Criteria for initiation of hemofiltration

- Oliguria (urine output < 100ml/6hr) unresponsive to fluid resuscitation
- Hyperkalaemia ([K^+]> 6.5 mmol/L)
- Severe acidaemia (pH<7.2)
- Urea > 25 mmol/litre
- Creatinine > 300 µmol/L
- Clinically significant organ oedema in the setting of AKI (e.g. lung)

Outcome measures

- Primary outcome measure*:
  Noradrenaline free time first week after randomization
- Secondary outcome measures:
  Change in the levels of three key cytokines IL-1, IL-6 and IL-10
- Additional outcomes: Changes in toll-like receptors, pro-apoptotic activity, time in ICU, time in hospital and survival

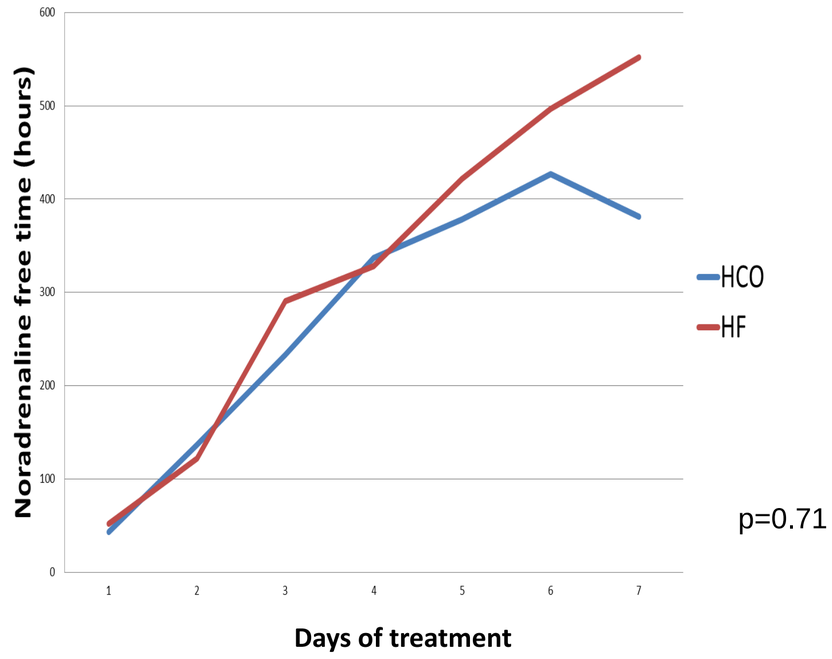
*Only results pertaining to primary outcome measure are displayed here

RESULTS

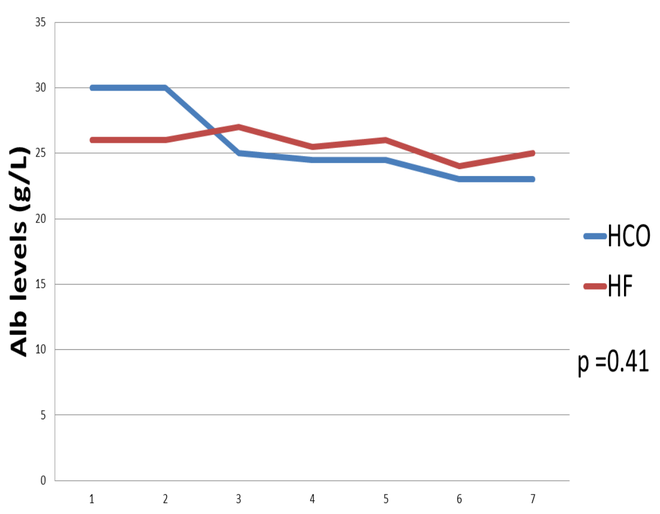
Baseline characteristics

	HCO (n=38)	HF (n=38)	p value
Age at adm	62.0	68.5	0.045
Sex: M (%)	17 (44.7)	26 (68.4)	0.037
Weight	78.8	80.1	0.748
APACHE 2	25.1	24.9	0.899
APACHE 3	94.1	89.5	0.518
Prev Creat	24.6	30.5	0.112
Creat	274	303	0.39
Urea	26.7	23.4	0.711
Serum Alb	29	27	0.095
NAdr start dose	17.4	16.3	0.7403

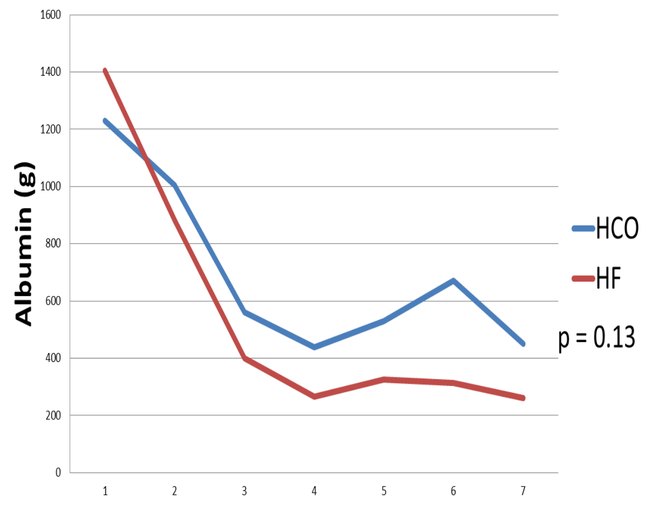
Cumulative noradrenaline free time



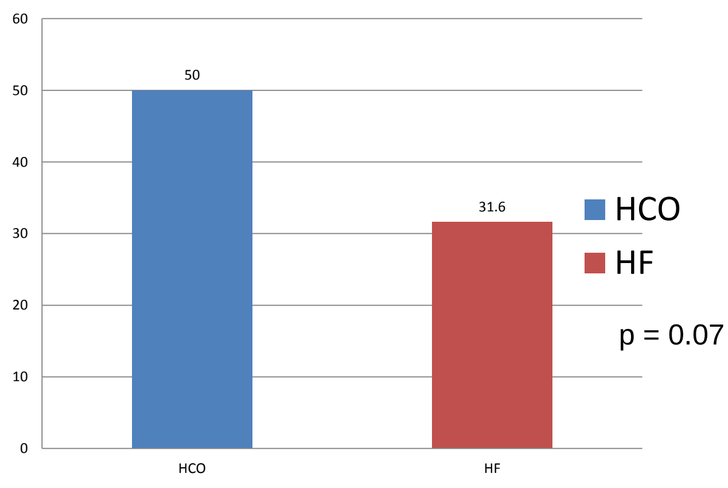
Median daily albumin levels



Total albumin administered per day



ICU mortality (%)



CONCLUSIONS

- There were some imbalances in randomization with regards to age and sex distribution
- No statistically significant differences in time off noradrenaline, daily albumin levels, amount of albumin administered or ICU survival
- No benefits of HCO hemofiltration could be identified in this study