Category :**Sepsis: basic mechanisms**

A190 - ***Microcirculatory dysfunction in sepsis-associated acute kidney injury is not equivalent to impaired tissue oxygenation***

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Introduction:

The mechanisms by which sepsis causes organ dysfunction are not well understood. Microcirculatory dysfunction has been proposed to cause sepsis-associated acute kidney injury (S-AKI). However, whether it induces S-AKI through tissue hypoperfusion or increased local inflammation remains unclear. We hypothesize that microcirculatory dysfunction can induce S-AKI in the absence of impaired renal cortical oxygenation

Methods:

C57Bl/6 mice (n=5-8/group) were randomly assigned to cecal ligation and puncture (CLP)-induced sepsis or sham surgery. We measured the following outcomes at 24h: renal injury using serum creatinine (sCr), systemic inflammation using IL-6, renal cortical oxygenation and mortality. Renal cortical oxygenation was measured by the phosphorescence quenching method using an established phosphorescent probe, Oxyphor PdG4, injected systemically, and an OxyLED fiber-optic phosphorometer. Partial pressures of oxygen (pO2) were measured in four locations of the kidney during 1 min each. Renal cortex microcirculatory flow was assessed using 2-photon intravital microscopy and quantified using the microvascular flow index (MFI)

Results:

CLP resulted in higher levels of sCr (CLP 1.66 vs Sham 0.98;p<0.001)**(Fig 1.1)**, Il-6 (CLP 7759.28 vs Sham 79.1;p=0.01)**(Fig 1.2)**, microcirculatory dysfunction evidenced by an MFI<2.5 (CLP 1.88 vs Sham 2.59;p=0.06)**(Fig 1.3)**, and higher mortality (CLP 64.2% vs Sham 0%;p<0.01)**(Fig 1.4)**. Importantly, the renal cortex oxygenation was higher in the CLP group (PO2: CLP: 53.7mmHg vs Sham 41.2mmHg;p<0.001)**(Fig 1.5)**.

Conclusion:

Sepsis induced a decrease in renal cortical microcirculatory blood flow concomitant with an increase in cortical partial pressure of oxygen. This suggesting that local regulation of microcirculatory blood flow relative to tissue demand was impaired and that this mechanism may contribute to the development of S-AKI. Further studies will need to address if this is secondary to a mechanism akin to tissue ‘hibernation’ vs. mitochondrial dysfunction.

Image :

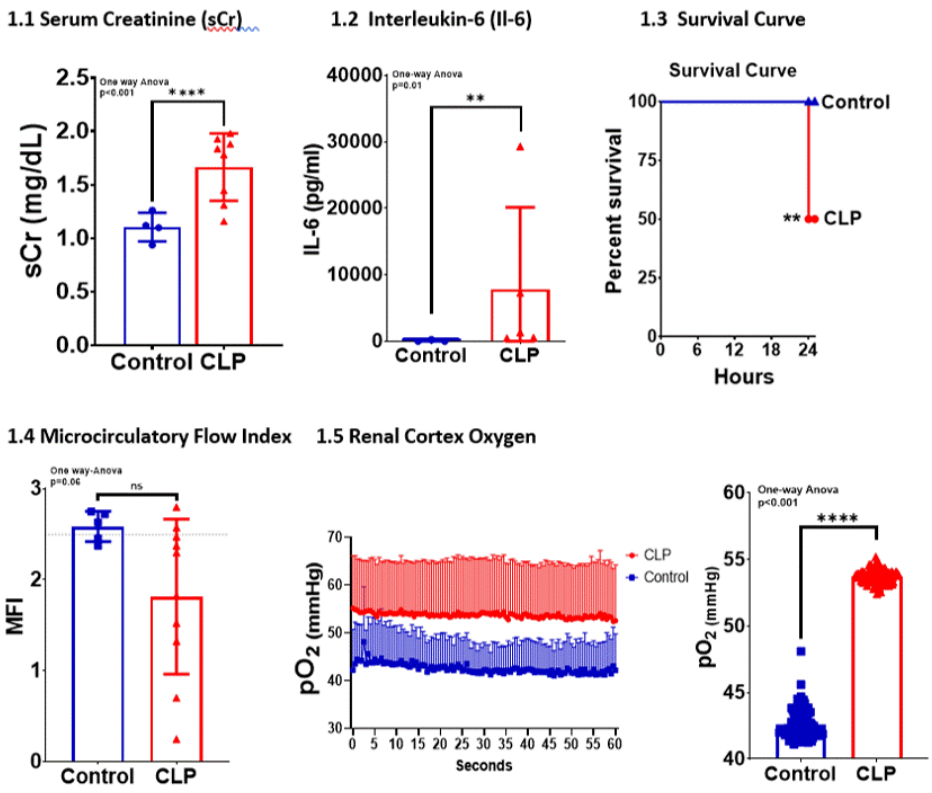
1.1 Serum Creatinine (sCr)
One way Anova
p<0.001
****
sCr (mg/dL)
2.5
2.0
1.5
1.0
0.5
0.0
Control CLP
1.2 Interleukin-6 (Il-6)
One-way Anova
p=0.01
**
IL-6 (pg/ml)
40000
30000
20000
10000
0
Control CLP
1.3 Survival Curve
Survival Curve
Percent survival
100
75
50
25
0
Control
** CLP
0 6 12 18 24
Hours
1.4 Microcirculatory Flow Index
One way-Anova
p=0.06
ns
MFI
3
2
1
0
Control CLP
1.5 Renal Cortex Oxygen
CLP
Control
pO2 (mmHg)
70
60
50
40
30
0 5 10 15 20 25 30 35 40 45 50 55 60
Seconds
One-way Anova
p<0.001
****
pO2 (mmHg)
60
55
50
45
40
Control CLP

Figure 1