REBOA Induces Medullary Hypoxia and Metabolic Failure While Hemorrhagic Shock Alone Predominantly Affects the Cortex

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BACKGROUND

Acute kidney injury (**AKI**) is frequent after hemorrhagic shock (**HS**) and potentiated by aortic occlusion (**AO**)

Renal **cortex** and **medulla** have distinct oxygenation and metabolic demands:

- **Medulla**: Greater tolerance to hypoxia due to glycolytic compensation
- **Cortex**: More vulnerable to hypoxia.

Prolonged ischemia during AO may exceed medullary oxygen reserve, resulting in region-specific metabolic failure

Hypothesis: Complete zone 1 AO induces disproportionate bioenergetic hit to the medulla, whereas HS alone primarily affects the cortex

METHODS

- 13 anesthetized adult Yorkshire pigs:
  HS (n=6) or HS+AO (n=7) (Fig.1)
- Continuous recording: renal tissue oxygen (**pO_2**) (HS: n=6, cortex & medulla; HS+AO: n=3, medulla only) (Fig.2,3)
- End of study: renal cortex and medulla mitochondrial O_2 consumption (**OXPHOS**) and tissue [ATP] (Fig.4)

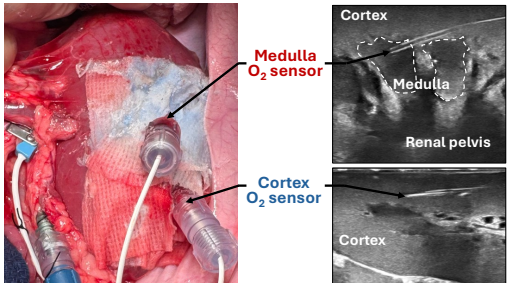

Figure 2: **Continuous renal oxygen monitoring.** Fiberoptic sensors were placed in the renal cortex (HS) and medulla (HS & HS+AO) to monitor regional pO_2.

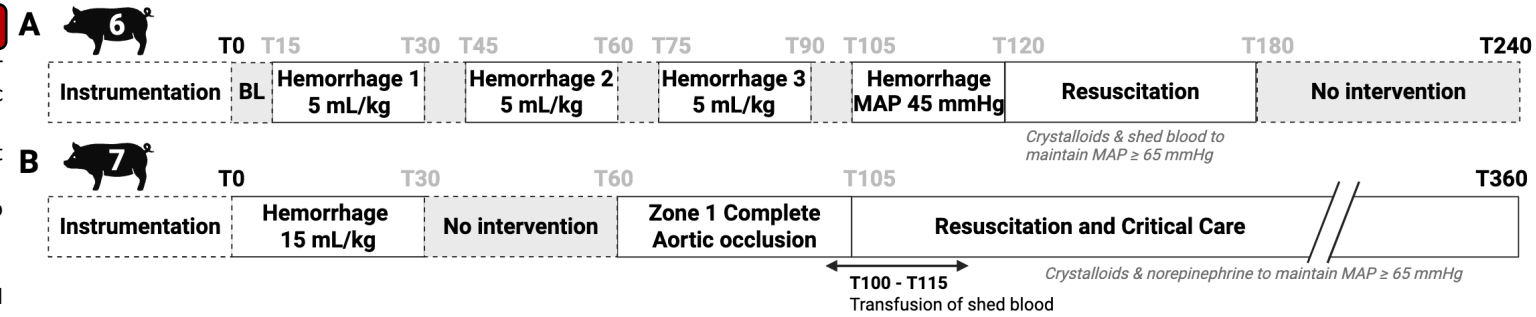

Figure 1: **Experimental protocol. A. HS model**: ATLS Class II hemorrhage was induced, followed by crystalloids and shed blood resuscitation to maintain a mean arterial pressure (**MAP**) ≥ 65 mmHg (n=6) (BL: baseline). **B. HS + AO model**: ATLS Class II hemorrhage was induced, followed by 45 min of complete zone 1 AO and resuscitation with crystalloids, shed blood, and norepinephrine to target MAP ≥ 65 mmHg (n=7).

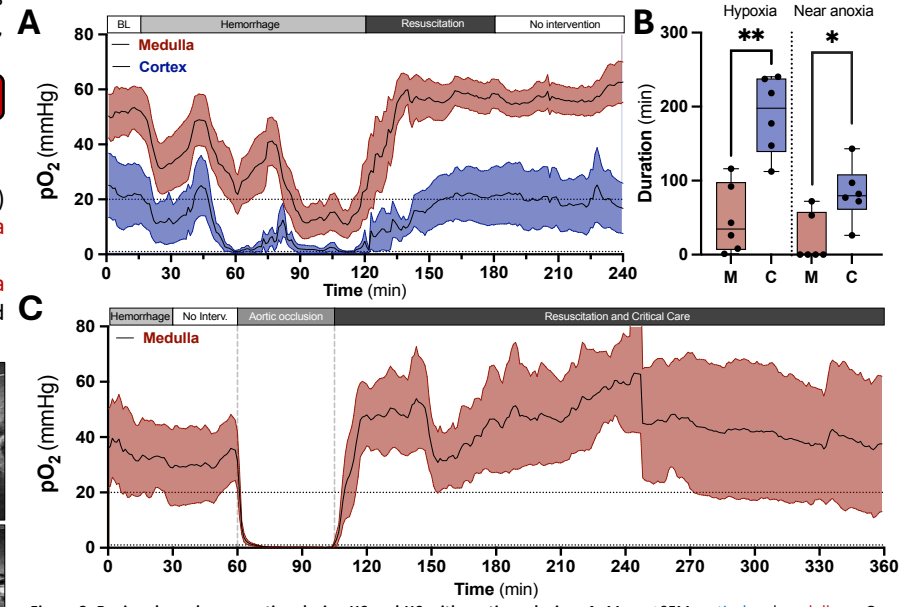

Figure 3: Regional renal oxygenation during HS and HS with aortic occlusion. A. Mean ±SEM cortical and medullary pO_2 over time during HS alone (n=6). **B.** Renal medulla (M) experiences shorter duration of hypoxia and near anoxia than the renal cortex (C) during HS (median [IQR]). **C.** Mean ±SEM medullary pO_2 over time during HS + AO (n=3). For A and C, the dotted lines represent hypoxia (20 mmHg) and near anoxia (1 mmHg) thresholds. *p < 0.05; **p < 0.01.

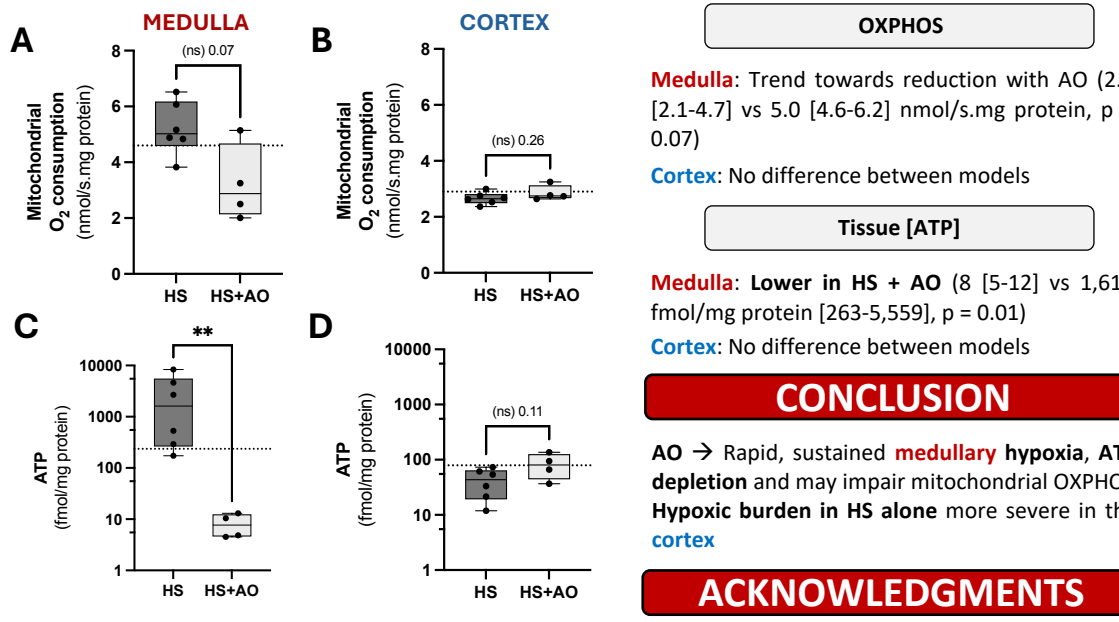

Figure 4: Regional bioenergetics during HS and HS+AO. A-B. Medullary mitochondrial oxidative phosphorylation capacity (OXPHOS) trended towards reduction in HS + AO, whereas cortical OXPHOS did not differ. C-D. Medullary ATP was significantly reduced with AO, whereas cortical ATP did not differ. Dotted lines represent median values from healthy animals for reference. Data presented as median [IQR].

RESULTS

Hypoxic burden

Medulla: **Shorter durations of hypoxia** (34 [6-98] vs 198 [138-238] min, p < 0.01) and **near anoxia** (0 [0-58] vs 80 [61-109] min, p = 0.01) than the **cortex** during HS alone

AO: Rapid **medullary** **pO_2 collapse to near anoxic levels** within 9 min, which persisted throughout occlusion. **Medullary** pO_2 recovered >20 mmHg within 6 [3-13] min of deflation

OXPHOS

Medulla: Trend towards reduction with AO (2.9 [2.1-4.7] vs 5.0 [4.6-6.2] nmol/s.mg protein, p = 0.07)

Cortex: No difference between models

Tissue [ATP]

Medulla: **Lower in HS + AO** (8 [5-12] vs 1,611 fmol/mg protein [263-5,559], p = 0.01)

Cortex: No difference between models

CONCLUSION

AO → Rapid, sustained **medullary** **hypoxia**, **ATP depletion** and may impair mitochondrial OXPHOS **Hypoxic burden in HS alone** more severe in the **cortex**

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