The JuxtaFlow® Renal Assist Device: A novel potentially renoprotective technology associated with reduced low urine oxygen burden in a swine CPB model

Stafford-Smith M MD,[1,3] Thomson S, MD,[2,3] Coles S, BS,[3] Tucker BJ, PhD.[3]

[1]Dept Anesthesiology, Duke Univ Med Ctr, Durham, NC, [2]Dept Medicine, UCSD, San Diego, CA, [3]3ive Labs, LLC. Roswell, GA.

INTRODUCTION

- The JuxtaFlow Renal Assist Device (JF-RAD; Figure 1) delivers mild negative pressure to the renal pelvises through ureteral catheters(with a coiled end) connected trans-urethrally to a pump.[1]
- While JF-RAD augments GFR, diuresis and natriuresis in volume-overload patients with cardiorenal syndrome,[2] its effects related to acute kidney injury (AKI) are unclear.
- AKI is a common complication of cardiac surgery, associated with low urine oxygen (puO2) levels (potentially related to renal medullary hypoxia).[3]

Therefore, in a mock cardiac surgery swine CPB model, we assessed for potential perioperative renoprotection related to continuous bilateral JF-RAD negative pressure treatment (Tx), using low puO2 as an AKI early biomarker.

METHODS

- IACUC appr., nine 50-65kg female pigs, general endotracheal anesthesia, arterial line monitoring
- Bilateral JF-RAD catheter placement (cystoscopic), with continuous -15 mm Hg (Tx group) or no negative pressure (control group).
- Periop periods included **baseline** (120min), **CPB** with heparin (left thoracotomy; ~120min; incl. Xclamp and cardioplegia), and **postCPB** (CPB separation, protamine and chest closure;120min).
- Measures, as summarized in Figure 2, included q60sec left and right JF-RAD catheter puO2
- Low puO2 (<40 and <35mmHg), as degree-duration AKI early biomarkers (mmHg.min), were contrasted between Tx and control groups; p< 0.05 considered significant.

Duke Anesthesiology
Duke University School of Medicine

RESULTS

- Nine pigs completed the protocol (Tx-5, control-4); one Tx animal excluded (puO2 started 80min after CPB initiation due to technical difficulties).
- Standard measures were similar between groups (Figure 2), and no left/right kidney puO2 differences were apparent among animals.
- Increased renal function trends were evident in Tx compared to control animals (UO, creatinine clearance, sodium excretion).
- No evidence of important hematuria.
- Low puO2 episodes (<40mmHg) were unilateral and bilateral, most frequent in the postCPB period. Each group had 9 episodes, but Tx group episodes were considerably shorter (av. 30 vs. 57min), resulting in significantly reduced low puO2 burden (p<0.02; Figure 3; 29.1 vs 83.4 mmHg.min/animal). Findings were similar in the <35mmHg analysis.

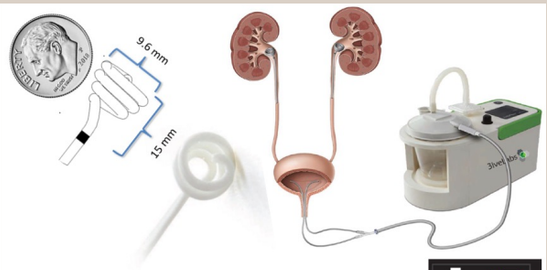

Figure 1: Overview of JuxtaFlow Renal Assist Device (JF-RAD)

Standard Measures:

Standard Perioperative
- vitals
- CPB flow
- hematocrit
- electrolytes
- arterial blood gas

Standard Kidney function
- creatinine clearance
- sodium excretion
- urine output (sum of JF-RAD, and Foley flows)
- urinalysis

Serum/urine IL6 levels

AKI Early Biomarker Measures:
puO2 - left and right JF-RAD catheters (q60sec)

Figure 2: Data collection was standardized for each animal through the experiment including standard and AKI biomarker determinations

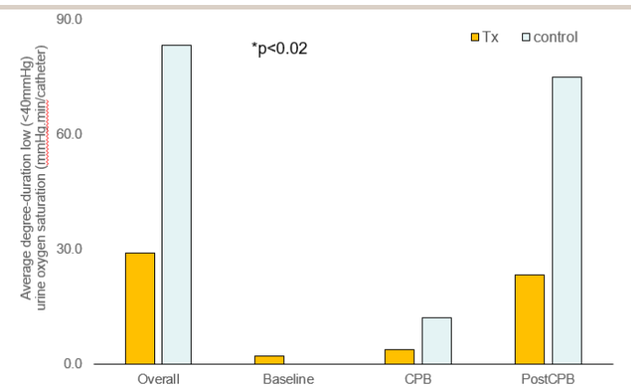

Figure 3: Burden of low urine oxygen levels (<40mmHg), an AKI early biomarker, in animals undergoing mock cardiac surgery with CPB was significantly lower with JF-RAD treatment (-15mmHg). Reanalysis with inclusion of available data from the excluded (Tx) animal further strengthened the primary finding (p=0.002)

CONCLUSIONS

In a mock cardiac surgery swine CPB model:

- JF-RAD negative pressure treatment significantly reduced low puO2 burden (a putative AKI early biomarker).
- In this small sample, catheter placement followed by heparin anticoagulation and CPB was not associated with important hematuria and did not have negative effects on renal function.

FUTURE DIRECTIONS

Such intriguing findings suggest JF-RAD negative pressure treatment may have renoprotective potential and support investigation in the context of cardiac surgery with CPB, particularly for cardiac surgery patients with high AKI risk.

References

1. Rao VS et al. Am J Physiol Regul Integr Comp Physiol 2021;321:R588-94
2. Asher J et al. PO199 2020 ASN Annual Meeting
3. Stafford-Smith M Anesthesiology 2021;135:380–1

Title: **The JuxtaFlow® Renal Assist Device: A novel potentially renoprotective technology associated with reduced low urine oxygen burden in a swine CPB model**

Stafford-Smith M MD,[1,3] Thomson S, MD,[2,3] Coles S, BS,[3] Tucker BJ, PhD.[3]

[1]Department of Anesthesiology, Duke University, Durham, NC. [2]Department of Medicine, University of California San Diego, San Diego, CA [3]3ive Labs, LLC. Roswell, GA.

Introduction: The JuxtaFlow Renal Assist Device (JF-RAD) delivers low, negative pressure to the renal pelvis through a ureteral catheter (with a coiled end) connected trans-urethrally to a pump.(1) Acute kidney injury (AKI), a common serious cardiac surgery complication, is associated with low urine oxygen (puO2) levels, potentially related to renal medullary hypoxia.(2) While JF-RAD may benefit patients with volume overload-related cardiorenal syndrome,(3) its relationship with AKI is unclear. Therefore, using a swine CPB model, and low puO2 as an AKI early biomarker, we assessed continuous perioperative JF-RAD negative pressure renal treatment (Tx).

Methods: With IACUC approval, 50-65kg female pigs with arterial line monitoring underwent JF-RAD catheter placement, either with continuous -15 mm Hg (Tx group) or no negative pressure (control group). For all animals, after a baseline period (~120min), cardiopulmonary bypass (CPB) with heparin anticoagulation was initiated through a left lateral thoracotomy (~120min; with a period of crossclamp and cardioplegia). CPB separation was followed by protamine and chest closure (postCPB; 120min). Measures included standard perioperative (vitals, CPB flow, hematocrit, electrolytes, arterial blood gas) and kidney function (urine output (UO), creatinine clearance, sodium excretion) variables, and q60sec left and right JF-RAD catheter puO2. UO was the sum of JF-RAD, and Foley flows. Serum/urine IL6 levels were also assessed. Since no AKI early biomarker benchmarks exist in swine, < 40 and < 35mmHg, as low puO2 degree-duration variables (mmHg.min), were contrasted between Tx and control groups; p< 0.05 considered significant.

Results: Nine pigs completed the protocol (Tx-5, control-4), however due to technical issues, puO2 data for 2 catheters (one Tx animal) started 80min after CPB initiation; while no episodes occurred, this animal was excluded from analysis. Measures were broadly similar between groups, including hemodynamic, CPB perfusion, lowest hematocrit, serum electrolytes, IL6, and blood gas variables. Averaged among catheters, there were also no apparent left/right puO2 differences. Interestingly, increased renal function trends were evident in Tx compared to control animals (UO, creatinine clearance, sodium excretion). Low puO2 episodes were distributed between unilateral and bilateral, and most frequent in the postCPB period. Although each group had 9 episodes, since Tx group episodes were shorter (av. 30 vs. 57min) this group had a notably reduced low puO2 burden (Figure; 29.1 vs 83.4 mmHg.min/animal; p< 0.02). Similar trends were evident in the < 35mmHg analysis.

Conclusion: In a swine CPB model, JF-RAD negative pressure treatment related to significantly reduced low puO2 burden (a putative AKI early biomarker). Such intriguing findings support more investigation into its renoprotective potential. Notably, in a small sample, catheter placement followed by heparin anticoagulation and CPB was not associated with hematuria, and did not have major effects on renal function.