Abstract Title: Urine oxygen tension monitoring as a measure of systemic perfusion
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Introduction

Acute kidney injury (AKI) is a common complication of cardiac surgery. There are currently no effective treatments for AKI, outside of expensive and complex clinical support options such as renal replacement therapy. Thus, injury prevention is the primary clinical goal. However, there are no validated tools or tests with robust prognostic value. Current diagnostic methods, which are based on changes in urine output or serum creatinine concentration, lead to a delayed diagnosis. Therefore, researchers have focused on identifying biomarkers to predict post-operative AKI earlier. However, these biomarkers change in response to renal injury, thus are not useful in preventing injury. Recent research has shown that urine oxygen partial pressure (PuO_2) can differentiate AKI from non-AKI patients during surgery [1]. It is essential for any monitor to be effective, to be tied to a proven clinical treatment. It is well understood that renal hypoxia contributes to AKI and that maintaining oxygen delivery above a critical threshold can prevent AKI [2], [3]. Thus, any potential interventions should focus on improving renal oxygenation. One possible method to improve renal oxygenation is increasing or maintaining systemic perfusion, as measured by mean arterial pressure (MAP). However, little research has been done connecting MAP and PuO_2 to measure perfusion of the renal medulla. The purpose of this preliminary work was to explore the relationship between PuO_2 and MAP. Understanding this relationship will help guide future studies focused on validating clinical interventions to prevent AKI.

Methods

Four pigs were anesthetized and instrumented. A novel device which measures PuO_2 in real-time was placed in line with a urinary catheter inserted into the bladder. MAP was monitored throughout each experiment. At time 0, hemorrhagic shock was induced by removing an estimated 25% of expected blood volume over 30 min through an arterial line. The subject then remained in a hypotensive state for 30 min. Following the hypotensive period, all animals underwent 45 minutes of resuscitative endovascular balloon occlusion of the aorta (REBOA). Animals received either a placebo or a novel drug. Before and during balloon deflation, the shed blood was transfused. 115 min after the start of the experiment, the animals entered the critical care phase. During this time, animals received a combination of balanced isotonic crystalloids (Plasmalyte 148) and norepinephrine according to a resuscitation algorithm to target a MAP > 65 mmHg . The relationships between the MAP and PuO_2 were qualitatively compared.

Results

During the hemorrhage and the following hypotensive period, the subjects did not produce enough urine to measure PuO2 accurately. However, during the critical care period, urine output was sufficiently large to monitor PuO_2 reliably. Figure 1 shows the PuO_2 and MAP during the resuscitation period of the 4 separate experiments. In pig 1, at approximately 155 min, there is a large increase in MAP, followed by a large increase in PuO_2. This delayed relationship

seems to be similar in pig 2. For example, at approximately 300 min, there is a drop in MAP, and shortly after, there is a drop in PuO_2. The relationship between PuO_2 and MAP is less clear for pig 3. However, it appears that there is a sharp increase in MAP followed by a gradual increase in PuO_2. In pig 4, it seems that changes in MAP are reflected by changes in PuO_2 with a slight delay similar to the prior studies.

Conclusion

Qualitatively, changes in MAP are reflected by changes in PuO_2 with a slight delay. Therefore, future work will focus on quantifying the delay between the two variables as well as the biological relevance of PuO_2 in diagnosing renal hypoxia early and as a potential goal-directed resuscitation tool.

References

1. Silverton NA, Lofgren LR, Hall IE, Stoddard GJ, Melendez NP, Van Tienderen M, Shumway S, Stringer BJ, Kang WS, Lybbert C, Kuck K. Noninvasive Urine Oxygen Monitoring and the Risk of Acute Kidney Injury in Cardiac Surgery. Anesthesiology. 2021 Sep 1;135(3):406-418.
2. Newland RF, Baker RA. Low Oxygen Delivery as a Predictor of Acute Kidney Injury during Cardiopulmonary Bypass. J Extra Corpor Technol. 2017;49(4):224-230.
3. Ow, CPC, Ngo, JP, Ullah, MM, Hilliard, LM, Evans, RG. Renal hypoxia in kidney disease: Cause or consequence?. Acta Physiol. 2018; 222:e12999.

Figure 1