Transdermal Measurement Detects GFR Changes during Cardiopulmonary Bypass: A Pre-Clinical Ovine Study

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Abstract

Background: Acute kidney injury (AKI) is associated with increased morbidity and mortality in patients undergoing cardiopulmonary bypass (CPB). AKI diagnosis currently depends on changes in serum creatinine and/or oliguria which are measured in the post-operative period. Relmapirazin (MB-102) is a fluorescent glomerular filtration rate (GFR) marker detectable by transdermal measurement; decreases in transdermal fluorescent intensity can be translated continuously in real-time to an accurate GFR (tGFR) in patients with stable chronic kidney disease (CKD). We aimed to leverage continuous tGFR assessment to assess for potential GFR changes associated with renal perfusion in a CPB ovine model.

Methods: Experiments were conducted over a three day period. The tGFR sensor was attached and the sequence of studies were: 1) injection before CPB distribution then transdermal fluorescent monitoring pre-CPB (1 hour), during CPB (4 hours), and after (1 hour) CPB and 2) injection for 4 hours POD1 & POD2. CPB started with a high perfusion rate, then transitioned to a low rate and then back to a high rate. Plasma samples were collected hourly for MB-102 measurement during CPB.

Results: Continuous transdermal fluorescence intensity and hourly plasma MB-102 concentrations are depicted in the Figure. Numeric clearance rates (fluorescent intensity/hour) extrapolated from decrease in transdermal fluorescence are depicted next to each phase of the experiment. Transdermal clearance rate was 0.72/hour on POD1 and 0.99/hour on POD2.

Conclusions: Transdermal MB102 detection MB102 of fluorescent intensity approximated plasma disappearance closely. Transdermal MB102 detection of fluorescent intensity change occurred instantaneously with changes in renal perfusion on CPB. We detected persistent decrease in transdermal clearance rates on POD1 with recovery to baseline clearance POD2. We suggest real-time transdermal GFR assessment is possible during CPB with our technology.

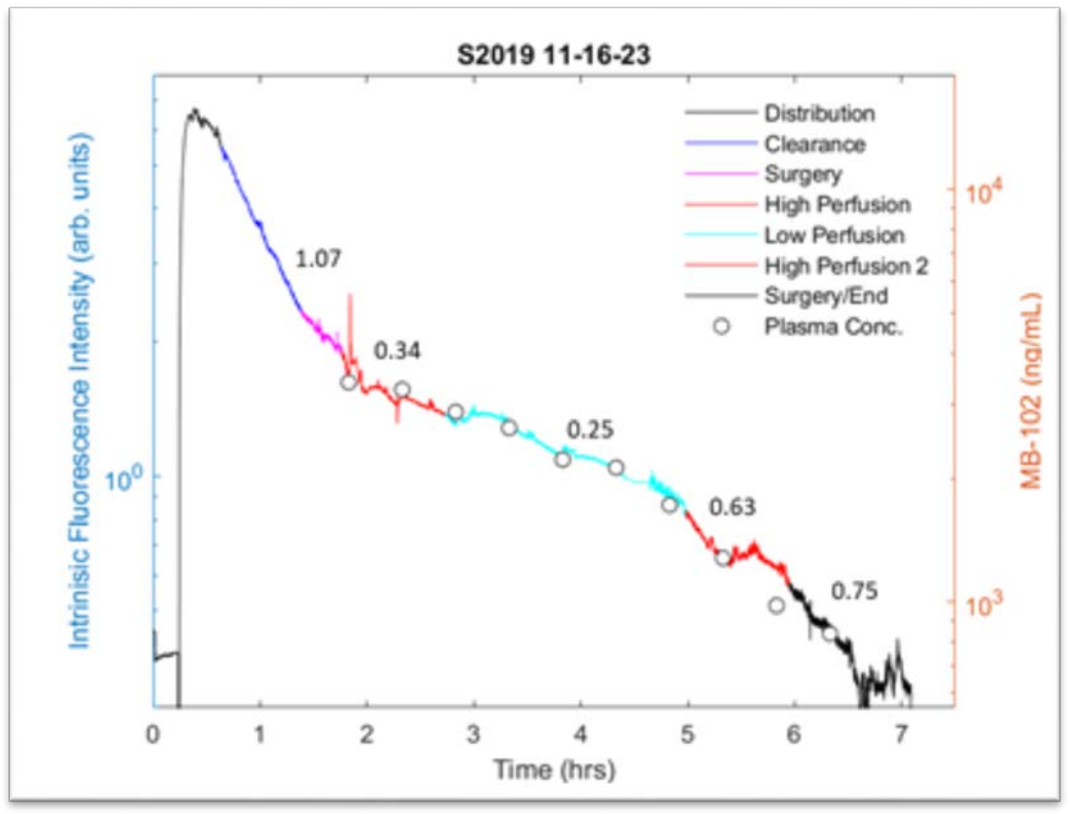
Introduction

- Acute kidney injury (AKI) is associated with increased morbidity and mortality in patients undergoing CPB and diagnosis currently depends on changes in serum creatinine and/or oliguria which are measured in the post-operative period.
- Relmapirazin (MB-102) is a fluorescent GFR marker detectable by transdermal measurement; decreases in transdermal fluorescent intensity can be translated continuously in real-time to an accurate GFR (tGFR) in patients with stable chronic kidney disease (CKD).
- We aimed to leverage continuous tGFR assessment to assess for potential GFR changes associated with renal perfusion in a well-established CPB ovine model.

Methods and Materials

- Experiments were conducted over a three day period
- The tGFR sensor was attached and the sequence of studies were:
  - injection before CPB distribution
  - transdermal fluorescent monitoring pre-CPB (1 hour), during CPB (4 hours) and after (1 hour) CPB
- CPB started with a high perfusion rate (80 ml/kg/minute), then transitioned to a low rate (40 ml/kg/minute)and then back to the high rate (80ml/kg/hour). Plasma samples were collected hourly for MB-102 measurement during CPB.
- POD1 & POD2 four-hour tGFR measurements

Results



Open circles represent plasma MB-102 concentrations

- Changes in MB-102 clearance rates are visible with major surgical events, and perfusion rate changes (**Figure and Table**)
- tGFR did not return to baseline until post-operative Day 2

	Intra-operative (hours)				Surgery End	POD1	POD2
	Pre-CPB	2-3	3-5	5-6			
Clearance rate (hours^{-1})	1.07	0.34	0.25	0.63	0.75	0.72	0.99

Discussion

- Transdermal detection MB102 of fluorescent intensity approximated plasma disappearance closely.
- Transdermal detection of MB102 fluorescent intensity change occurred instantaneously with changes in renal perfusion on CPB.
- We detected persistent decrease in transdermal clearance rates on POD1 with recovery to baseline clearance POD2.

Conclusions

- We suggest real-time transdermal GFR assessment is possible during CPB with our technology and has the potential to guide optimization of renal perfusion.

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