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Title: S-Nitrosylation status and its possible role in mitigating kidney hypoxia following CPB

Background: Impaired kidney function is frequently observed in heart surgery patients following cardio-pulmonary bypass. Previous studies by our group have linked acute reductions in nitric oxide bioactivity, the main regulator of tissue blood flow S-nitrosohemoglobin (SNO-Hb), to reductions in kidney oxygenation, blood flow and subsequent renal impairment. We hypothesized that components of the bypass procedure would reduce circulating SNO-Hb levels, with the magnitude of this reduction correlating with markers of kidney function and patient outcome.

Methods: After obtaining written informed consent, blood samples were obtained before and during bypass and on post-operative day (POD) 1. SNO-Hb levels, change in kidney function (estimated glomerular filtration rate; eGFR), and plasma erythropoietin (EPO) concentration were all measured. Status and outcome data were secured from the patients’ medical record.

Results: In the patients studied to date (n=28), a significant decline in SNO-Hb concentration by POD 1, correlated with ICU stay (R=-0.32). In addition, SNO-Hb and eGFR on PODs 1 & 2 directly correlated (R=0.48 and 0.30, respectively), i.e. lower SNO-Hb tracked with reductions in kidney function. Consistent with a presumed reduction in kidney oxygenation, plasma EPO levels were elevated at off pump and POD1. Elevated plasma EPO was inversely correlated with both SNO-Hb (R=-0.53) and eGFR (R=-0.55).

Conclusion: CPB decreases SNO-Hb and is associated with kidney dysfunction and worse patient outcome (increased ICU stay). While the mechanism for this decline remains to be determined, the results suggest that therapies directed at maintaining or increasing NO bioactivity could improve outcome in adult cardiac surgery patients.