2020 CAS Annual Meeting

Richard Knill Research Oral Competition (abstracts)

Contents

Cognitive and Behavioral Changes Following Exposure to Either Sevoflurane- or Propofol-Based Anesthesia in Children Undergoing MRI

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Introduction: Pediatric patients often require general anesthesia (GA) for magnetic resonance imaging (MRI). The effect of anesthetic agents on neurodevelopmental outcomes is unclear. Animal data supports detrimental effects, while human data has been inconsistent (1). Our study examined the effect of exposure to sevoflurane or propofol on cognitive and behavioral outcomes in children undergoing MRI.

Methods: Ethics approval was obtained from the local Research Ethics Board (REB16-0104). This study included children (N=50) between the ages of two and five years (American Society of Anesthesiologists Classification I-II), requiring GA for MRI. Prior to the MRI, parents completed reliable and validated questionnaires regarding their child's cognition (Behaviour Rating Inventory of Executive Function, Preschool Version [BRIEF-P]) (2) and behavior (Child Behavior Checklist 1.5-5 [CBCL]) (3). The BRIEF-P consists of 63 items rated on a Likert scale ranging from one (never) to three (often) that measures executive functioning across five domains: Inhibit, Shift, Emotional Control, Working Memory, and Planning/Organization, and forms one composite score (Global Executive Composite). The CBCL consists of 99 items rated on a Likert scale ranging from zero (not true) to two (very true or often true). The CBCL forms two broad domains, Internalizing (anxious, depressive, withdrawn and somatic symptoms) and Externalizing Problems (attention problems and aggressive behavior). Children were randomized via block design to receive either a sevoflurane- or propofol-based anesthetic. No long acting opioids or nitrous oxide were used. Airway management was at the discretion of the anesthesiologist. Questionnaires were repeated 90 days post-MRI. Linear mixed models were used to compare Global Executive Composite, Internalizing and Externalizing scores between children exposed to either sevoflurane- or propofol-based anesthesia. Paired t-tests were used to compare baseline to 90-day post-MRI Global Executive Composite, Internalizing and Externalizing scores in combined sevoflurane- and propofol-exposed groups.

Results: No differences in outcomes were observed between children exposed to sevoflurane- or propofol-based anesthesia. However, exposure to anesthetic (either sevoflurane or propofol) was associated with a moderate change in Global Executive Composite (t=-1.99[37], P=0.054, Cohen's d=0.32). Changes in the Global Executive Composite score were driven by changes in Working Memory (t=-2.09[37], P=0.043, Cohen's d=0.34), and Planning/Organization (t=-2.25(37), P=0.031, Cohen's d=0.37). Moreover, Internalizing scores were moderately changed (t=-2.01[38], P=0.051, Cohen's d=0.32), and Externalizing scores were significantly changed (t=-2.37[37], P=0.023, Cohen's d=0.38), following exposure to GA for MRI.

Conclusions: Exposure to GA for MRI, regardless of anesthetic type, was associated with worsening cognitive and behavioral outcomes in preschool-aged children. Future research utilizing a larger sample size is needed to determine whether these changes persist beyond 90 days post-MRI. Based on the cognitive and behavioral changes reported by parents, it may be advisable to reduce the frequency of MRIs and minimize anesthetic exposure in children less than 5 years of age.

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Competence of Anesthesiology Residents Following a Longitudinal Point-of-Care Ultrasound Curriculum: Early Results

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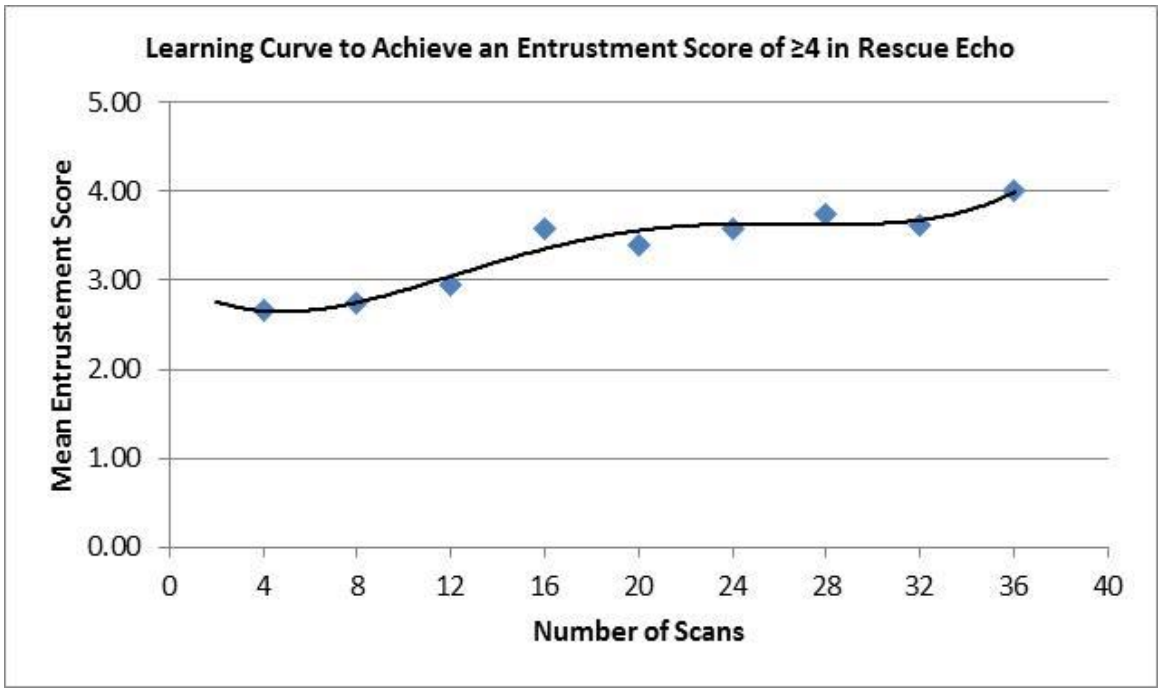
Introduction: Point-of-care ultrasound (POCUS) facilitates many diagnostic and procedural applications in anesthesiology.[1-3] Structured POCUS curricula have been shown to improve learner satisfaction, test scores, and affect clinical management,[4] but the learning curve towards competency and retention of competency over time remain unknown.

Methods: Ethics approval was waived by the local REB. We conducted a prospective observational study to determine whether anesthesiology trainees enrolled in a POCUS curriculum can achieve competency in POCUS skills and to plot the learning curve of trainees' competency using a POCUS-specific competency-based medical education assessment. The structured POCUS curriculum comprised of online lectures,[5] journal articles, live model scanning sessions, video review of cases, and development of a portfolio of supervised scans was delivered to residents in the Foundations and Core stages of training (PGY2-4) between January 2019 and February 2020. POCUS applications included Rescue Echo (focused cardiac ultrasound + lung for pneumothorax), lung ultrasound, Focused Assessment with Sonography in Trauma (FAST), abdominal aorta (AA), airway, and gastric ultrasound. POCUS scanning sessions on standardized patients were conducted in the simulation lab for 2.5 hours weekly; each resident attended 8 sessions (20 hours) per academic year. Timed image acquisition scores were obtained at each session by an experienced sonographer. Faculty evaluators completed the POCUS Skills Entrustment Scale[6] at each scanning session. Final entrustment scores reflected the lowest score obtained in the domains of insight, image acquisition, image interpretation, and clinical integration. Primary outcome was number of sessions and scans required to achieve average entrustment scores ≥4 ("may use independently"). Secondary outcomes include retention of skills at 3 months. The curriculum is ongoing.

Results: Twenty-five anesthesiology residents participated in the curriculum to date. An average POCUS entrustment score ≥4 was achieved in Rescue Echo after 9 sessions/36 supervised scans (14.5 dedicated curricular hours), and in lung ultrasound after 2 sessions/12 supervised scans (2 dedicated curricular hours). Residents have achieved average POCUS entrustment scores of 3 ("may use with indirect supervision") in FAST after 2 sessions/8 supervised scans (2 dedicated hours), and in AA ultrasound after 2 sessions/8 supervised scans (1 dedicated hour). Residents have achieved average entrustment scores of 2 ("may use only under direct supervision") in airway ultrasound after 2 sessions/8 supervised scans (2 dedicated hours) and in gastric ultrasound after 2 sessions/8 supervised scans (1 dedicated hour).

Conclusion: Our preliminary results suggest that anesthesiology residents participating in a structured longitudinal POCUS curriculum can achieve competence in Rescue Echo after 36 supervised curricular scans on standardized patients, and lung ultrasound after 12 supervised scans. These findings will be further informed by the final aspect of the

curriculum which will include observations and entrustment scores from clinically integrated POCUS scans and comprehensive summative assessments.



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Perioperative Outcomes of Nunavummiut Inuit in a Tertiary Care Hospital in Canada

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Introduction & Objectives: Structural aspect of the healthcare system, specifically limited access to surgical specialists and perioperative processes impact the outcomes and health resource use for Inuit surgical patients from Nunavut undergoing elective and emergency surgical procedures at a tertiary Canadian Hospital.

Methods: Ethics approval was received from the local Research Ethics Board. A retrospective cohort study was conducted of all inpatient surgery between 2011 and 2018 at a Canadian tertiary referral centre for eastern Nunavut. Primary outcome was a composite of in-hospital mortality or major complication. Secondary outcomes included postoperative hospital length of stay (LOS), readmissions within 30 days, institutional discharge and total hospitalization costs.

Results: There were 98,701 episodes of inpatient surgical care; 928 (0.9%) involved patients with Nunavut Inuit status. 159 (17.2%) of Nunavut Inuit patients died or suffered a post-operative complication, compared to 15,691 (16.1%) of the control group. After adjustment, individuals with Inuit status were significantly more likely to experience the primary outcome (OR 1.25, 95% CI 1.03 to 1.51; P=0.025). In subgroup analyses, the largest increase in risk of death or major complication for Nunavut Inuit status was associated with cancer surgery (OR 1.63, 95% CI 1.03 to 2.58: P=0.039) and elective surgery (OR 1.59, 95% CI 1.20 to 2.10; P= 0.001). Readmission occurred in 8.4% of Inuit patients vs. 6.9% (OR 1.4, 95% CI 1.09 to 1.77; P= 0.007); adverse discharge occurred in 21.8% of Inuit patients vs. 12.9% (OR 2.2, 95% CI 1.78 to 2.68; p=<0.0001); mean LOS for Inuit patients was 8.9 days vs. 6.6 days (difference 1.28; ratio of means 1.17 to 1.4); mean total cost for Inuit patients was $18,017 vs. $14,704 (difference 1.17; ratio of means 1.07 to 1.23).

Conclusions: Overall perioperative mortality and complications are 25% higher for Inuit patients from Nunavut at a major tertiary care hospital in Canada compared to the general population with increases in readmissions, adverse discharges, LOS and total cost. An overhaul of the perioperative systems involving multiple institutions and governments are required to address this inequity.

Table 1: Unadjusted and adjusted outcomes

Outcomes		Inpatient surgical episodes in patients without Inuit status **n = 97,773**	Inpatient surgical episodes in patients with Inuit status **n = 928**	Unadjusted effect* estimate **95% CI**	Adjusted effect* estimate **95% CI**
In-hospital mortality or major complication	n (%)	15,691 (16.1)	159 (17.2)	1.06 (0.89 – 1.27)	1.25 (1.03 - 1.51)
Readmission	n (%)	6,582 (6.9)	76 (8.4)	1.27 (0.99 – 1.62)	1.4 (1.09 - 1.77)
Adverse Discharge	n (%)	12,065 (12.9)	202 (21.8)	1.84 (1.56 – 2.17)	2.18 (1.78 – 2.68)
LOS	Mean (SD)	6.56 (11.98)	8.85 (14.41)		1.28 (1.17-1.4)
Total Cost	Mean (SD)	$14,703 ($25,884)	$18,017 ($30,832)		1.17 (1.07-1.23)

Note: SD = standard deviation; CI = confidence interval; *Effect estimate for in-hospital mortality or major complication, readmission and adverse discharge is an odds ratio; for LOS and cost is ratio of means.

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Prophylactic co-administration of oxytocin-ergonovine or oxytocin-carboprost versus oxytocin alone at cesarean delivery for labor arrest: A randomized controlled trial

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Introduction: Women with labor arrest have a higher predisposition to postpartum hemorrhage during cesarean delivery (CD) compared to non-laboring women, due to desensitization of oxytocin receptors from prior exposure to oxytocin during labor.[1] The objective of our study was to compare the efficacy of prophylactic administration of oxytocin-ergonovine (OE) vs. oxytocin-carboprost (OC) vs. oxytocin alone (O) at CD for labor arrest.

Methods: Ethics approval was obtained from the local REB. This was a prospective, double-blind, randomized controlled study on women undergoing CD for labor arrest under epidural analgesia. Women who received at least 4h of oxytocin for labor augmentation were included. They were randomized into 3 groups and prophylactically administered the study drugs after fetal delivery: OE group received IV oxytocin 5IU + IV ergonovine 0.25mg and IM placebo (1mL NS); OC group received IV oxytocin 5IU and IM carboprost 0.25mg (1mL); and O group received IV oxytocin 5IU and IM placebo (1mL NS). Intravenous drugs, diluted in 10mL saline, were administered over 1 min. Immediately after the administration of study drugs, oxytocin 40mU/min infusion was started in all groups. The obstetrician was asked to rate the uterine tone as satisfactory, equivocal or unsatisfactory at 3, 5 and 10 min after delivery. Additional uterotonics, if needed, were given, as per a planned regimen. The primary outcome was intraoperative need for additional uterotonics. Secondary outcomes included uterine tone, calculated blood loss and side effects. Multivariate logistic regression model was used to predict the need for additional uterotonics. Linear regression was used to develop a predictive model of calculated blood loss, and uterine tone was assessed using generalized estimating equations.

Results: Total 100 women were recruited (OE=33, OC=32, O=35). They had similar baseline demographic and obstetrical characteristics. The mean (SD) duration of oxytocin infusion during labor was 13 (7) h and the maximum rate was 16 (8) mU/min. Additional uterotonics were required in 35% cases after a mean (SD) of 9 (5) min after delivery, and did not differ across groups (p=0.94) (Table 1). The blood loss was not different across groups. There was a trend towards higher incidence of hypotension in O group (40%) compared to OE (15%) or OC (25%) (p=0.07), with significantly higher need for phenylephrine in O compared to OE group (adjusted p=0.004). Incidence of nausea and vomiting was not different across groups, however, there was a trend towards higher nausea in OE and OC groups than O group (P=0.06).

Discussion: We do not recommend the prophylactic use of combination of uterotonic drugs. Side effects were high in all groups, perhaps owing to high bolus doses of oxytocin. We suggest that oxytocin should be used as an infusion in appropriate doses and additional uterotonics used only as required.

Table 1. Primary and secondary outcomes across the study groups

Outcomes	Oxytocin+ Ergonovine (n=33)	Oxytocin+ Carboprost (n=32)	Oxytocin (n=35)	P value
Need for additional uterotonics (n%)	11 (33.3%)	11 (34.4%)	13 (37.1%)	0.943
More than one rescue uterotonic (n%)	6 (18.2%)	4 (12.5%)	2 (5.7%)	0.270
Rescue oxytocin (n%)	11 (33.3%)	11 (34.4%)	13 (37.1%)	0.943
Rescue ergonovine (n%)	4 (12.1%)	2 (6.3%)	0 (0.0%)	0.079
Rescue carboprost (n%)	4 (12.1%)	2 (6.3%)	2 (5.7%)	0.652
Rescue misoprostol (n%)	2 (6.1%)	2 (6.3%)	0 (0.0%)	0.387
Time (min) for first rescue (oxytocin) after delivery; mean (SD)	5.9 (2.9)	8.6 (6.3)	10.3 (5.3)	0.116
Time (min) for second rescue after delivery (ergonovine or carboprost); mean (SD)	12.3 (3.8)	18.0 (4.2)	24.0 (5.7)	0.104
Satisfactory uterine tone at 3 min after delivery (n%)	19 (57.6%)	21 (65.6%)	22 (62.9%)	0.814
Satisfactory uterine tone at 5 min after delivery (n%)	23 (69.7%)	24 (75.0%)	23 (65.7%)	0.707
Satisfactory uterine tone at 10 min after delivery (n%)	24 (72.7%)	25 (78.1%)	29 (82.9%)	0.656
Uterine massage (n%)	12 (36.4%)	9 (28.1%)	9 (25.7%)	0.629
Calculated blood loss, mL; mean (SD)	1145 (596)	1242 (609)	1180 (504)	0.789
Side effects				
Hypotension (< 20% baseline; n%)	5 (15.2%)	8 (25.0%)	14 (40.0%)	0.068
Phenylephrine amount (mg/mL; median [IQR])	0.0* [0.0 to 0.2]	0.2 [0.0 to 0.4]	0.2 [0.0 to 0.6]	0.006
Hypertension (> 20% baseline; n%)	5 (15.2%)	7 (21.9%)	6 (17.1%)	0.805
Tachycardia (> 30% baseline; n%)	11 (32.3%)	17 (53.1%)	17 (48.6%)	0.242
Chest pain (n%)	2 (6.1%)	1 (3.1%)	0 (0%)	0.311
SpO_2 < 90% (n%)	0 (0.0%)	3 (9.4%)	2 (5.7%)	0.234
Shortness of breath (n%)	1 (3.0%)	1 (3.1%)	1 (2.9%)	1.000
Nausea (n%)	25 (75.8%)	21 (65.6%)	17 (48.6%)	0.059
Vomiting (n%)	8 (24.2%)	13 (40.6%)	7 (20.0%)	0.149
Need for antiemetics (n%)	19 (57.6%)	20 (62.5%)	17 (48.6%)	0.500
Headache (n%)	3 (9.1%)	3 (9.4%)	0 (0.0%)	0.161
Flushing (n%)	4 (12.1%)	4 (12.5%)	2 (5.7%)	0.598

**Significant difference (P = 0.004) in phenylephrine administered post-delivery between oxytocin and oxytocin+ergonovine study groups.*

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Recovery of Psychomotor Function in Patients after Ambulatory Surgery Under General Anaesthesia With and Without Anxiolytic Premedication – A Randomized Investigation

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Introduction: The recovery of patients after general anaesthesia (GA) is usually evaluated by the scoring of clinical signs (1, 2). These scoring systems do not cover the assessment of psychomotor function, which may be compromised after GA and could lead to serious complications (2). The measurement of 4-choice reaction time (4CRT) is considered an established method to evaluate the psychomotor changes due to sedative medication (3) and was recently validated as the most convenient test to assess the recovery of psychomotor function in patients after GA (4). The aim of this study was to investigate psychomotor recovery after GA in patients with and without anxiolytic premedication in a relationship with conventional discharge scores.

Methods: Local ethics committee approved this investigation. 102 patients scheduled to ambulatory gynaecological surgery under standardized GA (duration<40 minutes) signed the informed consent form and were randomly assigned to receive 0.1 mg/kg oral midazolam (M group) or no (N group) for treatment of preoperative anxiety before surgery. Reaction times using the smartphone App “4CRT”, designed for this investigation (5), the grade of sedation (Richmond Agitation-Sedation Scale), discharge ability using Postanaesthesia Discharge Scoring System (PADSS), and hemodynamic parameters were recorded at baseline and at 6 time-points during the investigation and compared between the study groups. In another 22 female patients, who were recruited according to eligibility criteria and all received midazolam, the plasma concentration of this benzodiazepine was measured in addition to other outcome measures and its relationship with 4CRT was analyzed.

Results: Complete data from 94 randomized patients were available for evaluation. The M group showed prolonged reaction times compared to the N group 15 minutes following midazolam administration before surgery as well as at time-points 60 and 90 minutes following surgery ($P < 0.05$; Figure 1). The patients from both groups met the discharge criteria 60 minutes after surgery. The reaction times of the M group returned to baseline 90 minutes after surgery. Reaction times of the N group returned to baseline 45 minutes after surgery but only 23 of the 45 patients in the N group met the discharge criteria at that time. Plasma midazolam concentration of 22 patients was correlated with 4CRT only at time-point 15 minutes following benzodiazepine administration ($r = 0.57$; $P = 0.006$).

Conclusion: After short-term general anaesthesia, the psychomotor function recovers faster than the ability to discharge according to PADSS. Premedication with midazolam prolongs the recovery of psychomotor function without delaying the clinical ability to discharge. The recovery of psychomotor function in patients after long (> 60 minutes) general anaesthesia should be controlled using 4CRT in the future.

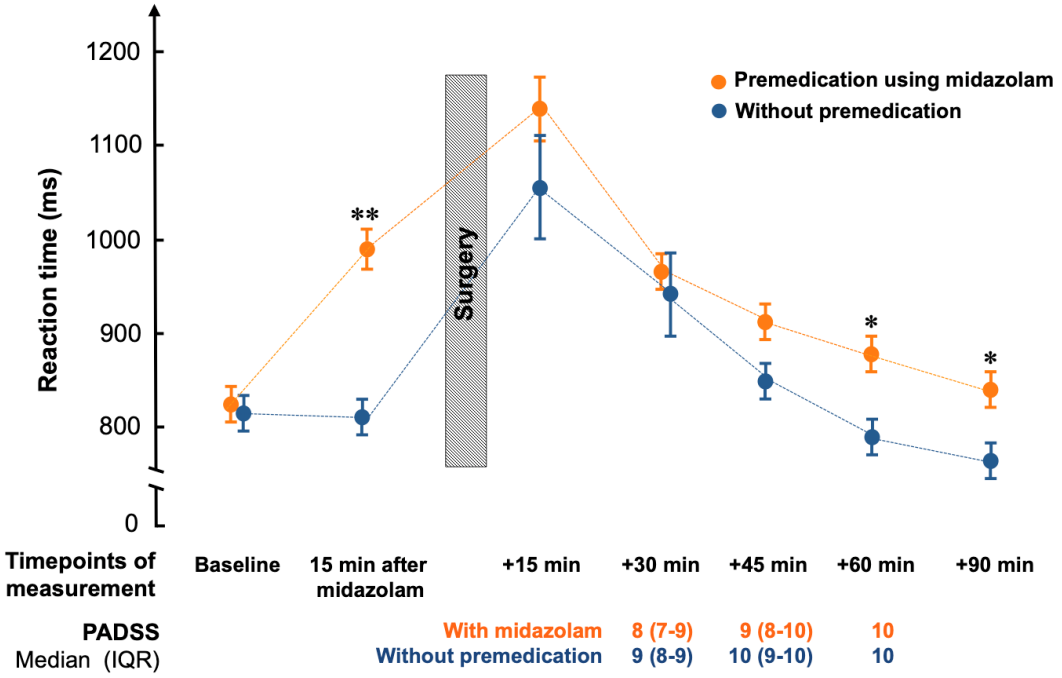

Figure 1: Reaction times measured using the 4-CRT App, given as the mean ± standard error of mean at various times during the investigation. Comparison between the groups was performed using Student's *t*-test for paired observations with Bonferroni-adjustment for multiple comparisons. * $P < 0.05$; ** $P < 0.0001$.

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Renal Tissue PO2 Measurements Reflect the Degree of Acute Hemodilution and Demonstrate a Negative Impact of Starch Colloid on Renal Oxygenation

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Introduction: The role of starch colloid solutions in optimal fluid resuscitation remains controversial. Recent clinical trials have demonstrated the potential for starch mediated renal toxicity in critical care and surgical settings (1, 2). We assessed the impact of colloid (starch and albumin) and crystalloid (saline) hemodilution protocols in terms of their impact on cardiac output (CO) and renal tissue oxygen tension ($P_{kt}O_2$). We hypothesized that hemodilution with starch colloid would negatively impact $P_{kt}O_2$ relative to other solutions following acute hemodilution.

Methods: Ethics approval was obtained from the local REB, male Sprague Dawley rats (n=77, 484 ± 64g) were randomly assigned to undergo hemodilution with saline (40% estimated blood volume, 3:1 vol:vol), 6% hydroxyethyl starch (30 or 40% EBV, 1:1), 5% albumin (40% EBV, 1:1) or time-based control. Heart rate, MAP and rectal temperature were monitored continuously. Arterial blood gases, cooximetry data and echocardiograms were performed at baseline, 30 and 60 minutes post-hemodilution. $P_{kt}O_2$ was measured continuously on the left kidney by a phosphorescence quenching method using Oxyphor PdG4 as an oxygen probe. Kidneys were harvested after 60 minutes post-hemodilution determine RNA levels (qPCR) for erythropoietin (EPO), and other hypoxia-induced molecules. Data was tested for normality and analysis was performed by ANOVA or ANCOVA. ($p<0.05$ was taken to be significant)

Results: All measurements were comparable between groups at baseline. After hemodilution, the hemoglobin concentration (Hb) decreased in all treatment groups; reaching nadir values near 70g/L (40% albumin and starch) and 90g/L (40% saline or 30% starch) respectively ($p<0.005$ for both). Mean arterial pressure (MAP) decreased slightly after hemodilution, but without significant difference between groups. Arterial pO_2 was not significantly different between groups. Changes in cardiac output were transient and values were comparable between groups after hemodilution. The final $P_{kt}O_2$ was lowest after 40% hemodilution with starch (34.1 ± 6.6 mmHg) and significantly different relative to 40%

hemodilution with saline (46.9 ± 5.9 mmHg; $p<0.02$). A significant linear relationship between changes in $P_{kt}O_2$ relative to changes in C_aO_2 was observed. The slope of the relationship was significantly steeper for starch hemodilution relative to albumin and saline (0.333 versus 0.222 respectively, $p<0.008$). Renal tissue mRNA levels for EPO were increased substantially after starch and saline hemodilution ($p<0.05$).

Conclusion: Kidney tissue oxygen tension decreased in proportion with the drop in C_aO_2 following hemodilution regardless of the diluent. Hemodilution with starch resulted in a more pronounced reduction in $P_{kt}O_2$ and an increase in EPO mRNA levels, indicative of impaired microvascular oxygen delivery and accentuated tissue hypoxia. The more favorable hemodynamic and $P_{kt}O_2$ responses following hemodilution with albumin warrant further investigation.

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