Title: EFFECT OF CEREBRAL PERFUSION PRESSURE DURING CARDIOPULMONARY BYPASS ON NEURO-PSYCHIATRIC OUTCOME FOLLOWING CORONARY ARTERY BYPASS GRAFTING

Authors: T.E. Stanley, III, M.D., L.R. Smith, Ph.D., W.D. White, MPH, L. Morrison, M.S., J. Blumenthal, Ph.D., E.J. Burker, M.S., S. Schniebolk, MPH, M. Newman, M.D., N. Croughwell, CRNA, J.G. Reves, M.D.

Affiliation: Division of Cardiac Anesthesia, Department of Anesthesiology and Department of Psychiatry, The Heart Center, Duke University Medical Center, Durham, North Carolina 27710

Introduction. Previous studies have demonstrated no correlation between mean arterial pressure (MAP) during cardiopulmonary bypass (CPB) and gross changes in neurologic function postoperatively. However, no studies have compared cerebral perfusion pressure (CPP = MAP-CVP) during CPB and discriminating tests of neuropsychiatric (Npsych) function. We examined this relationship in patients undergoing coronary artery bypass grafting (CABG).

Methods. The day prior to elective CABG, enrolled patients had neurologic examination and Npsych testing (NP1). These tests included psychomotor (Digit Span and Symbol, DIG_{1-3}, Trail Making Test, TMT) and memory (Randt Short Story, RSS_{1-4}, Benton Visual Retention, BVR) measures, and tests for negative emotion (State Trait Anxiety Inventory, STAI, Center for Epidemiology Studies of Depression Scale, CESD). Patients with a history of cerebrovascular disease, alcoholism, or psychiatric illness were excluded. All intraoperative anesthesia patient data were recorded using the Arkive® Patient Information Management System (Diatek®, Inc.) at a one minute resolution. General anesthesia was induced and maintained with midazolam and fentanyl. CPB using moderate hypothermia was instituted. After CABG and after rewarming to 36° C., CPB was discontinued. The remainder of the patient's management was routine. One day prior to discharge, Npsych testing was repeated (NP2). Mean and minimum CPP during CPB (CPPavg, CPPmin, respectively) and the duration of CPB in which CPP was less than 50 mm Hg (TM50) were determined from the Arkive-recorded data. NP2 and NP1 data were compared, and variables that showed a significant decrement were analyzed with the CPP data using Pearson's correlation coefficients.

Results. 19 patients were evaluated. Patient data are listed in Table 1. NP2 tests were performed 5 - 11 days after CABG. No gross neurologic deficits occurred. Five Npsych tests demonstrated a significant decrease. Table 2 lists the correlation coefficients of these Npsych tests with the CPP indices. There were no significant associations of any CPP value with the abnormal Npsych studies.

Discussion. These data demonstrate that CPP is not associated with any of the decrements in postoperative neurologic function documented in these patients. Even with the duration of CPP under 50 mm Hg averaging 32 minutes, no dysfunction was associated with perfusion pressure. This information suggests that decreased Npsych test performance is related to factors other than CPP, and that there may be no basis for the recommendation that CPP be maintained ≥ 50 mm Hg in this population of patients.

Table 1. *Patient Demographics and Intraoperative Variables*

	Mean ± SD	Range
Age (years)	68 ± 3	64 - 75
CPB time (min)	112 ± 34	53 - 194
Temperature, CPB (avg.,°C.)	31.6 ± 1.4	28.7 - 33.5
CPPavg (mm Hg)	54 ± 6	47 - 65
CPPmin (mm Hg)	27 ± 10	5 - 42
TM50 (min)	32 ± 17	10 - 67

Table 2. *CPP versus decreased Npsych parameters*
Pearson correlation coefficients

	CPPavg	CPPmin	TM50
DIG_1	0.20	-0.01	0.01
DIG_3	0.12	0.08	-0.39
RSS_2	-0.11	0.27	0.24
BVR	0.24	0.26	-0.41
STAI	0.09	0.10	0.20

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Title: Esmolol and Controlled Hypotension: Adverse Effects on Oxygen Extraction.

Authors: T.J. Quinn, M.D. , V.M. Zayas, M.D., K. LeDonne, M.D., M. McDonald, B.S., T. Pickering, M.D.

Affiliation: Department. of Anesthesiology, Hospital for Special Surgery, N. Y., N. Y. 10021

Esmolol (E) is used to attenuate the sympathetic and renin responses to controlled hypotension (CH) with sodium nitroprusside (SNP). We studied the effect of increasing doses of E on oxygen consumption (VO2), delivery (DO2), and plasma renin activity (PRA) during SNP CH.

After IRB approval and informed consent, thirty one consecutive patients (ages 10-73, mean=36) undergoing posterior spine fusion without contraindications to the use of CH or beta blockade were studied. Arterial and oximetric pulmonary artery catheters(Spectramed) were placed preoperatively. General anesthesia was induced with fentanyl (7 mcg/kg), thiopental (3 mg/kg) and vecuronium (0.15 mg/ kg), and maintained with N2O(66%), and fentanyl (1.5 mcg/ kg/h). All patients received E at 100, 200, and 400 mcg/ kg/min (E100, E200, E400) in random sequence following an initial loading dose of 0.5 mg/kg. SNP was titrated to maintain MAP at 55mmHg. Hemodynamics (HR, MAP, CI, CVP, PCWP) and blood samples for Hgb, PRA, lactate, arterial and mixed venous oxygen saturation were collected at baseline (after induction, prior to incision and CH), and after a minimum of 45 min at each E infusion level. VO2, DO2, and oxygen extraction ratio (OER=VO2/DO2) were calculated using cooximetry data (Corning 2500). Results were analyzed using ANACOVA and ANOVA for repeated measures (alpha set at 0.05).

One patient developed HR<50 and prolonged PR interval after E loading and was withdrawn from the study. Two other patients had E400 withheld because OER exceeded 0.50 at E200. OER increased significantly with doses above E100, despite a trend towards lower VO2 at higher E doses. DO2 fell with increasing E doses, reaching statistical significance only at E400. A downward trend in heart rate at higher E doses was not significant. Serum lactate, while statistically higher during CH, remained in the normal range and did not vary with E dose. There was no effect of E dose on PRA during CH. When analysed for covariance, increasing age was associated with significantly higher OER at doses above E100 (p=0.016).

We conclude that E doses greater than 200 mcg/kg/min during CH with SNP offer no advantage in suppressing PRA and are deleterious to total body oxygen balance. The use of E doses greater than 200 mcg/kg/min may warrant monitoring of CI and/or mixed venous oxygen saturation, particularly in elderly patients.

		---------- CH ----------		
Mean ± SD	Baseline	E100	E200	E400
VO2 ml/min	143±38	153±36	143±38	140±31
DO2 ml/min	530±105	583±210	499±159	432±138*
HR bpm	63±12	68±12	66±12	63±12
OER	.27±.05	.28±.08	.31±.10 *	.35±.11 *†
Lactate mM/l	1.3±.4	1.7±.8 *	1.6±.6 *	1.8±.8 *
PRA ng/ml/h	7.6±7.5	8.5±14.2	5.8±6.6	8.5±12.4
CI l/min/M2	2.3±.6	2.7±.9 *	2.4±.8	2.1±.6 §

* p<0.05 vs baseline †p<0.05 vs E200 § p<0.05 vs E100