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Predicting the Limits of Cerebral Autoregulation During Cardiopulmonary Bypass

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Abstract

Background—Mean arterial blood pressure (MAP) targets are empirically chosen during cardiopulmonary bypass (CPB). We have previously shown that near-infrared spectroscopy (NIRS) can be used clinically for monitoring cerebral blood flow autoregulation. The hypothesis of this study was that real-time autoregulation monitoring using NIRS-based methods is more accurate for delineating the MAP at the lower limit of autoregulation (LLA) during CPB than empiric determinations based on age, preoperative history, and preoperative blood pressure.

Methods—Two hundred thirty-two patients undergoing coronary artery bypass graft and/or valve surgery with CPB underwent transcranial Doppler monitoring of the middle cerebral arteries and NIRS monitoring. A continuous, moving Pearson's correlation coefficient was calculated between MAP and cerebral blood flow velocity, and between MAP and NIRS data to generate mean velocity index and cerebral oximetry index. When autoregulated, there is no correlation between cerebral blood flow and MAP (i.e., mean velocity and cerebral oximetry indices approach 0); when MAP is below the LLA, mean velocity and cerebral oximetry indices approach 1. The LLA was defined as the MAP where mean velocity index increased with declining MAP to ≥ 0.4 . Linear regression was performed to assess the relation between preoperative systolic blood pressure, MAP, MAP in 10% decrements from baseline, and average cerebral oximetry index with MAP at the LLA.

Results—The MAP at the LLA was 66 mmHg (95% prediction interval, 43 to 90 mmHg) for the 225 patients in which this limit was observed. There was no relationship between preoperative MAP and the LLA ($p = 0.829$) after adjusting for age, gender, prior stroke, diabetes, and hypertension, but a cerebral oximetry index value of >0.5 was associated with the LLA ($p=0.022$). The LLA could be identified with cerebral oximetry index in 219 (94.4%) patients. The mean difference in the LLA for mean velocity index versus cerebral oximetry index was -0.2 ± 10.2

mmHg (95% CI, -1.5 to 1.2 mmHg). Preoperative systolic blood pressure was associated with a higher LLA ($p=0.046$) but only for those with systolic blood pressure ≤ 160 mmHg.

Conclusions—There is a wide range of MAP at the LLA in patients during CPB making estimating this target difficult. Real-time monitoring of autoregulation with cerebral oximetry index may provide a more rational means for individualizing MAP during CPB.

Because cerebral blood flow autoregulation is functional during cardiopulmonary bypass (CPB) using α -stat pH management, arterial blood pressure targets are empirically chosen often to a mean arterial blood pressure (MAP) of 50 mmHg depending on patient age, preoperative blood pressure, or medical history.^{1,2} The foundation of this practice, though, is based on data that are more than 15 years old and derived from patients who were generally younger and had fewer co-morbid conditions than patients in current practices.³⁻⁵ The accuracy of empiric targeting of MAP for identifying a pressure above the lower limit of autoregulation (LLA) in clinical practice is not known. Other data suggest a benefit of higher MAP during CPB on myocardial and neurologic outcomes, but these results have limitations and have not been independently reconfirmed.⁶⁻⁹ Importantly, whether the practice of targeting low MAP during CPB is appropriate for the increasing number of elderly patients with cerebral vascular disease is not known.^{10,11} Our group, in fact, has found a high frequency of hypoperfusion type “watershed” strokes after cardiac surgery that were associated with MAP during CPB that was ≥ 10 mmHg lower than before CPB.¹¹

Real-time autoregulation monitoring can be accomplished by the continuous calculation of the correlation between transcranial Doppler-measured cerebral blood flow velocity of the middle cerebral artery and cerebral perfusion pressure (termed mean velocity index).¹²⁻¹⁴ Our group has demonstrated in laboratory experiments and in patients undergoing cardiac surgery that near-infrared spectroscopy (NIRS) signals provide an acceptable surrogate for monitoring changes in cerebral blood flow for autoregulation monitoring.¹⁵⁻¹⁷ The latter approach might provide a method for individualizing MAP during CPB without the need for specialized equipment and without the limitations of transcranial Doppler monitoring (e.g., need for trans-temporal insonating window, interference from electric cautery, movement artifact, etc).

The hypothesis of this study was that real-time autoregulation monitoring using NIRS-based methods is more accurate for delineating the MAP at the LLA during CPB than empiric determinations based on age, preoperative history, and preoperative arterial blood pressure.¹⁸⁻²⁰

Methods

The prospective observational cohort study was approved by the IRB of The Johns Hopkins Medical Institutions and written informed consent was provided by all patients. Patients undergoing cardiac surgery with CPB were enrolled from December 8, 2008 to October 4, 2010. Patients in the current study included some patients previously enrolled in a prospective study evaluating the accuracy of NIRS-based cerebral blood flow autoregulation monitoring during CPB.^{16,21}

Intraoperative Care

Patient care during surgery has been reported and included direct radial artery blood pressure and nasal temperature monitoring.^{16,21} The patients received midazolam, fentanyl, and isoflurane for anesthesia and pancuronium for skeletal muscle relaxation. Nonpulsatile CPB flow between 2.0 and 2.4 L/min/m² was used with a membrane oxygenator and a 27 μ m arterial line filter. Alpha-stat pH management was used. Isoflurane concentrations during

CPB were kept between 0.5% and 1.0% on a vaporizer connected to the oxygenator inflow. Hemoglobin level and arterial blood gases were measured after tracheal intubation, 10 min after initiation of CPB, and then hourly. Gas flow to the oxygenator during CPB was manipulated to maintain normocarbida based on continuous in-line arterial blood gas monitoring or arterial PaCO₂ results. During CPB, blood pressure targets, transfusion of packed red blood cells, and the rate of rewarming were based on standard clinical practice.

Autoregulation Monitoring

The patients were attached to NIRS monitors (INVOS, Somanetics, Inc., Boulder, CO) via self-adhesive sensors placed on the right and left forehead. Transcranial Doppler monitoring of the right and left middle cerebral artery (Doppler Box, DWL, Compumedics, USA, Charlotte, NC) was performed using two 2.5-MHz transducers fitted on a headband. Our signal acquisition and analysis methods have been described.^{16,21} Digitized arterial blood pressure, transcranial Doppler, and NIRS signals were processed with a personal computer using ICM+ software (University of Cambridge, Cambridge, UK). Filtering of the arterial blood pressure, Doppler, and NIRS signals was performed to limit analysis to the frequency of slow vasogenic waves (0.05 Hz to 0.003 Hz), which are relevant to autoregulation.^{22,23} Exclusion of wave components outside this bandwidth eliminates confounding inputs from the analysis. Specifically, low-pass filtering eliminates respiratory and pulse frequencies which cause false positive readings of passivity; high pass filtering eliminates drifts associated with hemodilution at the onset of bypass, blood transfusions, cooling, rewarming, etc. These drifts are not vasogenic in nature, and confound the interpretation that passivity is loss of autoregulation. Low pass filtering was accomplished with non-overlapping 10-second time-integrated mean values. High pass filtering was performed with a detrending cutoff set at 0.003 Hz to remove slow, nonvasogenic drifts.

Next, a continuous, moving Pearson's correlation coefficient between MAP and cerebral blood flow velocity and NIRS signals was performed generating the variables mean velocity index and cerebral oximetry, respectively. As previously described, consecutive, paired, 10-second averaged values from 300 seconds duration were used for each calculation, incorporating 30 data points for each index.^{16,21} Blood pressure in the autoregulation range is indicated by a mean velocity index value that approaches zero while a mean velocity index value approaching +1 indicates dysregulated cerebral blood flow (i.e., flow and MAP not correlated or correlated, respectively). Similarly, values for cerebral oximetry index approaching 1 and zero indicate dysregulated and autoregulated cerebral blood flow, respectively. Clinicians in the operating room had access to the raw NIRS data for clinical management but they were blinded to the autoregulation monitoring results.

Data Analysis

Right and left transcranial Doppler recordings and NIRS data were used for analysis unless only unilateral recordings were available. To assess the LLA, values for mean velocity index were categorized in 5 mmHg bins of MAP for each patient. The mean velocity index cut-off indicating the LLA is not clearly known but it is likely to be between 0.25 and 0.5.^{14,21,24} For the purpose of this study we defined the LLA as the MAP where mean velocity index incrementally increased from < 0.4 to ≥ 0.4. When mean velocity index was ≥ 0.4 at all MAP during CPB, the autoregulation threshold was defined as that MAP where mean velocity index had the lowest value. Baseline blood pressure was defined as that measured during the preoperative evaluation that was performed either the day before surgery or the morning of surgery.

Multiple linear regression was used to estimate the effect of demographic variables (age, gender), medical history (diabetes, hypertension, and prior cerebrovascular accident),

preoperative blood pressure (MAP, systolic blood pressure, pulse pressure), and time-averaged cerebral oximetry index characteristics on MAP at the LLA. Relationships between continuous predictors and MAP at the LLA were examined using scatter plots with nonparametric smoothers. Linear splines with relevant knots were used in the models to incorporate deviations from linear relationships. Model fit and homoscedasticity were evaluated by plots of residuals against predicted values. Plots of residuals against quintiles of normal distribution were used to assess normality of residuals. Undue influence on model fit was assessed by Cook's D statistic. In the sensitivity analyses, the points with high influence were excluded. The differential effect of hemodynamic indices by age and gender was checked by including interaction terms and testing their significance at 0.05 level. Due to relatively low proportion of missing values and the hypothesized missing data mechanism, complete case analysis was used under the assumption of missing completely at random.²⁵ A receiver operator characteristic (ROC) curve was constructed comparing 10% decrements in MAP from the baseline measurements for identifying the LLA during CPB. Statistical analysis was performed with Stata software version 11 (StataCorp LP, College Station, TX).

Results

The demographic and operative data for the 232 enrolled patients are listed in Table 1. The average age of the patients was 66 ± 12 years. Thirty-nine percent of patients were > 70 years of age and 8% were older than 80 years. The patients had a high frequency of co-morbid conditions including a history of stroke in 8.6% of patients. Carotid artery ultrasound was obtained before surgery based on clinical indications in 121 patients revealing a high prevalence of carotid artery atherosclerosis. A clear autoregulation threshold was not observed in 7 patients. This might indicate that MAP was above our definition of the LLA throughout CPB. Physiologic variables during CPB are listed in Table 2. The MAP at the LLA was 66 mmHg (95% prediction interval, 43 to 90 mmHg) for the 225 patients in which this limit was observed. The distribution of MAPs at the LLA is shown in Figure 1.

The results of the linear regression models are listed in Table 3. For some of the adjusted models deviations from homoscedasticity were revealed. Therefore, the models were re-run using robust variance estimates (Huber-White estimator of variance).^{26,27} Because the results and conclusions were not altered, we present the results from the regression with model-based standard errors. We did not find major deviations from normality or highly influential observations. There was no relationship between preoperative MAP and the MAP at the LLA ($p = 0.829$) after adjusting for age, gender, prior stroke, diabetes, and hypertension. The model predicts that there is nonlinear relationship between cerebral oximetry index and average MAP at the LLA after adjusting for age, gender, prior stroke, diabetes and hypertension. When < 0.5 , there is no linear relationship between cerebral oximetry index and MAP at the LLA. However, for values of cerebral oximetry index ≥ 0.5 , the adjusted model estimates that patients with 0.1 higher cerebral oximetry index have 3.6 mmHg lower average MAP at the LLA threshold (95% CI: 0.5 to 6.7 mmHg lower, p -value = 0.022). There was a nonlinear effect of preoperative systolic blood pressure on MAP at the LLA. For patients whose preoperative systolic blood pressure is ≤ 160 mmHg, the model estimates that those who have 5 mmHg higher preoperative systolic blood pressure have 0.6 mmHg higher MAP at the LLA (95% CI: from 0.01 to 1.1 mmHg, p -value = 0.046) after adjustment for age, gender, and co-morbidities. For patients whose preoperative systolic blood pressure is > 160 mmHg, there was a trend for higher preoperative systolic blood pressure to be associated with lower MAP at the LLA ($p = 0.118$). Diabetes, hypertension, or prior cerebrovascular accident were not associated with MAP at the LLA.

The MAP at the LLA for men and women with various conditions is shown in Figure 2. Our results suggest that men might have higher MAP at the LLA than women ($p=0.068$). The MAP at the LLA was not different between patients with or without hypertension, diabetes, or prior stroke regardless of age or gender. There was no difference in MAP at the LLA for patients with a pulse pressure ≥ 70 mmHg ($n=73$, 31.5% of patients) compared with the reference groups with pulse pressure < 50 mmHg (71.0 mmHg vs 67.3 mmHg, $p=0.113$).

The sensitivity, specificity, and area under the ROC curve for various cut-offs of MAP from preoperative baseline measurement for predicting the LLA are shown in Table 4. A 15% decrement in MAP from baseline had a 91% sensitivity for detecting the MAP at the LLA but the specificity was low (37%). The area under the ROC curve for this model was low (0.7354). In contrast, 140 (60.3%), 196 (84.5%), and 219 (94.4%) of the 232 patients had a LLA determined with cerebral oximetry index within 5 mmHg, 10 mmHg, and 15 mmHg of that determined by mean velocity index, respectively. The mean difference in the LLA for mean velocity index versus cerebral oximetry index was -0.2 ± 10.2 mmHg (95% CI, -1.5 to 1.2 mmHg). Cerebral oximetry index detected a LLA in all but 5 patients using our criteria. In these patients a LLA would have been present with a cerebral oximetry index threshold ≤ 0.3 . In 7 patients mean velocity index remained < 0.4 with declining MAP and, thus, a clear autoregulation threshold was not observed. In these patients a LLA was detected with our cerebral oximetry index threshold.

Thirteen patients suffered a perioperative stroke. The LLA for patients with stroke (74 ± 15 mmHg, 95% confidence intervals, 63 to 84 mmHg) tended to be higher than for patients not suffering a stroke (66 ± 12 mmHg, 95% confidence intervals 65 to 68 mmHg, $p=0.054$). There was no difference in the percentage of time spent below the LLA during CPB for patients with and without stroke (mean difference -4.6% , 95% CI: -23.3% to 14% , $p=0.359$). Compared with patients without a stroke, those with a stroke were more likely to have diabetes ($p=0.029$), have a history of stroke ($p=0.005$), and have longer duration of CPB ($p<0.0001$) and aortic cross-clamping ($p=0.0284$).

Discussion

In a cohort of mostly elderly and high-risk patients we found that the average MAP at the LLA during CPB was 66 mmHg. There was much variability in the LLA, though, with a 95% prediction interval between 43 and 90 mmHg. We further found that predicting the MAP at the LLA during CPB based on clinical history and preoperative arterial blood pressure was imprecise. In contrast to clinical predictors, we found that the NIRS-based cerebral oximetry index was significantly associated with the MAP at the LLA. Women tended to have a lower MAP at the LLA than men while patients with a stroke tended to have a higher MAP at the autoregulation threshold than those without stroke.

The current understanding of cerebral blood flow autoregulation in patients during CPB is mostly based on data derived using ^{133}Xe washout or N_2O dilution methods.^{1,2,4,5,28,29} These studies were often limited to pooled data or to a limited number of discrete measurements made when CPB flow was maintained and MAP manipulated with vasoactive drugs. Based on these data, a basic tenet of patient management during CPB has been that a MAP as low as 20 mmHg to 55 mmHg may be tolerated since autoregulation is intact and CPB flow is relatively constant.^{1,2,4,5,28,29} However, this practice was challenged by Gold et al⁶ who reported that targeting a MAP of 80 to 100 mmHg during CPB was associated with a lower combined frequency of stroke and myocardial outcomes than when MAP was targeted at 50 to 60 mmHg. The external validity of these results were questioned due to the small sample size ($n=248$) and an unexpectedly high rate of stroke in the control group (7.2%).⁷ Nonetheless, there is currently little evidence to guide clinicians on the most

appropriate MAP targets during CPB. This may have implications for current practices that include increasing proportions of elderly patients with cerebrovascular disease.^{10,11}

Continuous cerebral blood flow autoregulation monitoring as used in this study provides an individual estimate of autoregulation based on fluctuations in MAP that occur during the course of surgery. This approach allows perhaps for a more precise determination of the LLA than discrete and intermittent measurements. The continuous nature of the measurement is important as cerebral blood flow autoregulation is dynamic and potentially influenced by many perioperative perturbations, including rewarming from hypothermia, volatile anesthetics (dose dependently), and anemia.^{30,31} Our observations suggest that predicting the exact MAP target during CPB to remain above the LLA is difficult based on clinical history and preoperative blood pressure measurement. Although there was a positive relationship between the MAP at the LLA and systolic blood pressure (i.e., higher MAP at the LLA with increasing systolic blood pressure), this association was limited to patients with systolic blood pressure ≤ 160 mmHg and the association was less robust compared with cerebral oximetry index ≥ 0.5 (Table 3). The sensitivity of predicting the MAP at the LLA based on preoperative MAP had wide confidence intervals and low specificity (Table 4). Furthermore, the low area under the ROC curve suggests that factors other than preoperative MAP influence the ability to predict this end-point. Ultimately, the exact tolerance of error in predicting MAP during CPB will depend on the patient population. Our observations suggest that a MAP in the usual clinical range of 50 to 70 mmHg during CPB might result in cerebral blood flow being pressure passive in some patients predisposing to cerebral hypoperfusion.^{10,11} At the same time, maintaining empirically high MAP targets may unnecessarily expose some patients with a low LLA to higher cerebral blood flow potentially increasing cerebral embolic load and predisposing to cerebral edema.^{5,32}

Transcranial Doppler monitoring during cardiac surgery is associated with many known limitations including the need to frequently readjust the transducer and interference from electric cautery. These limitations are particularly germane before CPB when continuous monitoring is difficult during harvest of the internal mammary artery when electrocautery use and patient repositioning are frequent. For this reason, we do not provide estimates of the LLA before CPB for comparing transcranial Doppler results with NIRS data. In contrast, NIRS output, and hence autoregulation monitoring, is continuous throughout surgery and it is not susceptible to the same limitations of transcranial Doppler. Thus, in clinical practice MAP targets derived from NIRS would be available before CPB and even after surgery when patient movement may limit transcranial Doppler monitoring.

We did not find a difference in the MAP at the LLA for patients with or without diabetes, hypertension, or prior stroke. These conditions have been suggested to result in a rightward shifted LLA.¹⁸⁻²⁰ Our comparison group was not a normal control group, but rather included patients with cardiovascular disease and its associated endothelial dysfunction that results in abnormalities in microcirculatory process maintaining cerebral blood flow autoregulation.³³ We did observe that patients suffering stroke had a higher MAP at the LLA compared with patients without a stroke (74 ± 15 mmHg versus 66 ± 12 mmHg, $p=0.054$). These findings are tempered, though, by the small number of patients in our study that does not allow for risk adjustments. Our use of arterial blood pressure measurement from the preoperative evaluation might not represent a true baseline measurement. This measurement, however, is what clinicians usually evaluate when planning perioperative care. Thus, our methods represent a pertinent clinical practice situation.

In our study we used a time-domain approach for cerebral blood flow monitoring that assumes that changes in transcranial Doppler-measured blood flow velocity over short periods of time result from changes in MAP. This method does not require assumptions of

stationarity as with frequency domain methods (e.g., based on phase shifts, transfer functions) of cerebral blood flow autoregulation assessments that are not consistently present during surgery and in critical care settings.¹⁴ The signal-to-noise ratio with our approach, however, is less than with other cerebral blood flow autoregulation testing methods because the output (cerebral blood flow velocity) and input (MAP) contain both noise and autoregulation information. Time averaging of the data and focusing on slow wave fluctuations in cerebral blood flow velocity (0.003 to 0.04 Hz) are used to improve the signal-to-noise ratio. Changes in cerebral blood flow velocity in this frequency range are believed to represent autoregulatory compensations to slow hemodynamic oscillations.³⁴⁻³⁶

Our results support our prior findings showing that NIRS can be exploited for autoregulation monitoring.^{16,24,37,38} In a piglet laboratory model we found that cerebral oximetry index was significantly correlated with cerebral blood flow autoregulation monitoring based on laser Doppler methods.²⁴ In that study, and in an investigation of neurosurgical patients, NIRS waveforms at frequencies lower than 0.04 Hz had high coherence with laser Doppler or transcranial Doppler-measured cerebral blood flow velocity, respectively.^{24,35} We have found significant coherence between slow waves of cerebral blood flow velocity and NIRS in patients during CPB.¹⁶ These data together suggest that cerebral blood flow autoregulation monitoring is possible in patients during CPB using NIRS. Basing MAP targets during CPB on real-time cerebral blood flow autoregulation data, compared with the current standard of care of empirically derived targets, might ensure adequate cerebral blood flow during surgery and lead to improved neurological outcomes.

As mentioned, mean velocity index indicating the limits of autoregulation is likely to be between 0.25 and 0.5.^{14,21,24,39} We acknowledge that the use of a mean velocity index of ≥ 0.4 for defining the LLA is somewhat arbitrary. This is in part due to the nature of autoregulation whereby vasoreactivity responsible for mediating this response continues until extremely low blood pressure.¹⁴ That is, a discrete threshold where cerebral blood flow becomes completely blood pressure-passive is unlikely. Thus, the correlation between cerebral blood flow and MAP does not precipitously increase to values closer to 1 at some MAP. Rather, mean velocity index incrementally increases with declining MAP. Thus, our approach may have resulted in some error in depicting an exact MAP at the LLA if this occurred at a lower or higher mean velocity index in some patients. Regardless, the value of mean velocity index we chose was associated with delirium in patients with sepsis.³⁵ The effects of nonpulsatile CPB flow on cerebral autoregulation are not known. Studies in animals did not show a convincing effect of nonpulsatile CPB on global cerebral blood flow or regional oxygen saturation.⁴⁰ Further, the issue of nonpulsatile versus pulsatile CPB perfusion would likely affect autoregulation determinations by either the continuous methods we used or the intermittent measurements used with ¹³³xenon washout or the Kety-Smith method. Regardless, arterial blood pressure is rarely truly “nonpulsatile” during CPB due to small variations in blood pressure from the non-occlusive roller pump variation of flow. Finally, our methods use averaged blood pressure and cerebral blood flow velocity in the calculations that would reduce the influence of nonpulsatile CPB.

In conclusion, there is a wide range of MAP at the LLA in patients during CPB making estimating this target difficult. Real-time monitoring of autoregulation using cerebral oximetry index may provide a more rationale means for individualizing MAP during CPB.

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Figure 1. Number of subjects versus the mean arterial blood pressure at the lower limit of cerebral blood flow autoregulation during cardiopulmonary bypass based on the transcranial Doppler-determined mean velocity index.

Figure 2.

Mean arterial blood pressure (MAP) at the lower limit of cerebral blood flow autoregulation for men and women based on age for patients with and without a history of diabetes, hypertension, or stroke. The error bars are the 95% confidence intervals. The LLA was defined as the MAP associated with an increase in the mean velocity index to ≥ 0.4 (see Methods section in the text). The MAP at the LLA tended to be higher for men than women ($p=0.081$).

Table 1

Demographic and medical data for the enrolled patients. Data are listed as the number and percent of patients unless otherwise indicated.

Variable	All Patients n=232
Age (years) (mean±SD, range)	66± 11 (45-89)
Male	183 (78.9%)
Female	49 (21.1%)
Hypertension	156 (67.2%)
Diabetes	64 (27.6%)
COPD	24 (10.3%)
Peripheral Vascular Disease	28 (12.1%)
Congestive Heart Failure	36 (15.5%)
Prior Myocardial Infarction	73 (31.5%)
Prior stroke	20 (8.6%)
Current Tobacco Smoker	37 (15.9%)
Left Ventricular Ejection Fraction <30%	28 (12.1%)
Left Carotid Artery Stenosis	(n=121)
< 50%	6 (5.0%)
50-69%	99 (81.8%)
70-99%	13 (10.7%)
>99%	3 (2.5%)
Right Carotid Artery Stenosis	(n=121)
< 50%	4 (3.3%)
50-69%	105 (86.8%)
70-99%	9 (7.4%)
>99%	2 (1.6%)
	1 (0.8%)
Medications	
Aspirin	156 (67.2%)
Beta-Blockers	144 (62.1%)
“Statin” drugs	145 (62.5%)
Calcium Channel Blockers	38 (16.4%)
ACE Inhibitors	73 (31.5%)
Surgery	

Variable	All Patients n=232
Reoperation	12 (5.2%)
CABG	148 (63.8%)
CABG/AVR	23 (9.9%)
CABG/MVR or Repair	5 (2.1%)
AVR	34 (14.7%)
MVR or Repair	12 (5.2%)
Ascending Aorta Replacement	4 (1.7%)
Valve Sparing Aortic Root Replacement	6 (2.6%)
Cardiopulmonary Bypass Duration (min)	235±114
Aortic Cross-Clamp Duration (min)	75±30

COPD=chronic obstructive pulmonary disease; ACE=angiotensin converting enzyme; CABG = coronary artery bypass graft; CPB=cardiopulmonary bypass; AVR=aortic valve replacement; MVR=mitral valve replacement.

Table 2

Physiologic variables and cerebral measurements during cardiopulmonary bypass. Values are listed as mean $\pm$ SD.

Variable	Result
Mean arterial pressure	74 $\pm$ 7.3
pH	7.39 $\pm$ 0.04
PaCO ₂ (mmHg)	39.7 $\pm$ 3.6
PaO ₂ (mmHg)	253.0 $\pm$ 45.3
Hemoglobin (gm/dL)	9.1 $\pm$ 1.8
Middle cerebral blood flow (cm/s)	
Left	34.8 $\pm$ 11.7
Right	34.5 $\pm$ 11.1
Left Frontal NIRS O ₂ Saturation	
Left	57.3 $\pm$ 11.3
Right	57.0 $\pm$ 9.8
Temperature during CPB	32.9 $\pm$ 2.3 $^{\circ}$ C (range 25-36.6)

CPB=cardiopulmonary bypass; NIRS= near-infrared spectroscopy

Table 3

Linear regression results of variables in relation to defining the lower limit of cerebral blood flow autoregulation based on mean velocity index monitoring.

Predictor	Unadjusted Model				Adjusted Model*			
	Beta	95% CI	p-value		Beta	95% CI	p-value	
Preoperative MAP (per 5 mmHg increments)	0.01	-0.6, 0.6	0.983		0.1	-0.5, 0.7	0.829	
Preoperative systolic blood pressure (per 5 mmHg increments)								
≤160 mmHg	0.5	-0.03, 1.0	0.066		0.6	0.01, 1.1	0.046	
>160 mmHg	-1.2	-2.6, 0.2	0.094		-1.1	-2.6, 0.3	0.118	
Pulse Pressure								
>70 mmHg	2.7	-1.6, 7.1	0.214		3.6	-0.9, 8.1	0.113	
>60 to 70 mmHg	0.9	-4.1, 5.8	0.728		1.7	-3.4, 6.9	0.502	
>50 to 60 mmHg	-0.9	-6.0, 4.1	0.715		-0.8	-5.9, 4.3	0.761	
≤50 mmHg (reference group)								
Average cerebral oximetry index (per 0.1 increment)	0.06	-0.8, 1.0	0.903		-0.2	-1.1, 0.8	0.708	
≤ 0.5	-3.7	-6.8, -0.6	0.020		-3.6	-6.7, -0.5	0.022	
>0.5								
Age (per 1 year increment)	0.01	-0.1, 0.2	0.851		0.01	-0.1, 0.2	0.860	
Male gender	4.0	-0.3, 8.4	0.068		3.9	-0.5, 8.3	0.081	
Diabetes	-0.9	-4.5, 2.6	0.608		-0.8	-4.5, 2.9	0.677	
Hypertension	-0.6	-4.2, 3.1	0.758		-0.5	-4.3, 3.4	0.812	
Prior cerebrovascular accident	1.9	-3.7, 7.4	0.515		1.8	-3.9, 7.5	0.534	

* adjusted for age, gender, prior stroke, presence of diabetes and hypertension

MAP = mean arterial blood pressure

Sensitivity, specificity and area under the receiver operator characteristic (ROC) curve for various cut-offs of mean arterial blood pressure (MAP) from preoperative baseline measurement for predicting the lower limit of cerebral blood flow autoregulation.

Table 4

MAP Decrement from Baseline	Sensitivity	95% CI	Specificity	95% CI	Area Under ROC
>15%	91%	87% to 93%	37%	32% to 41%	0.7354
>25%	71%	66% to 76%	66%	61% to 70%	
>35%	42%	37% to 47%	88%	85% to 91%	