The effect of blood pressure on cerebral outcome in a rat model of cerebral air embolism during cardiopulmonary bypass

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Objective: Higher mean arterial pressure during cardiopulmonary bypass may improve cerebral outcome associated with cerebral air embolism by increasing emboli clearance and collateral flow to salvage the ischemic penumbra. However, this may come at the expense of increased delivery of embolic load. This study was designed to investigate the influence of mean arterial pressures on cerebral functional and histologic outcome after cerebral air embolism during cardiopulmonary bypass in an established rat model.

Methods: Male Sprague–Dawley rats were exposed to 90 minutes of normothermic cardiopulmonary bypass with 10 cerebral air embolisms (0.3 μL/bolus) injected repetitively. Rats were randomized to 3 groups (n = 10, each) that differed in mean arterial pressure management during cardiopulmonary bypass: 50 mm Hg (low mean arterial pressure), 60 to 70 mm Hg (standard mean arterial pressure), and 80 mm Hg (high mean arterial pressure). Neurologic score was assessed on postoperative days 3 and 7 when cerebral infarct volumes were determined. Cognitive function was determined with the Morris water maze test beginning on postoperative day 3 and continuing to postoperative day 7.

Results: Neurologic score was better in high and standard mean arterial pressure groups versus low mean arterial pressure groups. High mean arterial pressure resulted in shorter water maze latencies compared with standard and low mean arterial pressure on postoperative days 6 and 7. Total infarct volume and number of infarct areas were not different among groups.

Conclusions: The use of higher mean arterial pressure during cardiopulmonary bypass in a rat model of cerebral air embolism conveyed beneficial effects on functional cerebral outcome with no apparent disadvantage of increased delivery of embolic load. Maintaining higher perfusion pressures in situations of increased cerebral embolic load may be considered as a collateral therapeutic strategy. (J Thorac Cardiovasc Surg 2011;142:424-9)

Cerebral injury, ranging from neurocognitive dysfunction to overt stroke, remains as a significant cause of morbidity and mortality after cardiac surgery using cardiopulmonary bypass (CPB).[1] Although considered multifactorial, the most importantly cited etiologic factors are cerebral macro- and microembolism and hypoperfusion.[2,3] Among them, the principal cause of neurocognitive impairment is believed to be cerebral microembolization with the majority being gaseous, which invariably occurs during CPB.[4,5] Accordingly, both experimental and human studies have demonstrated a significant correlation between the number, as well as the volume, of cerebral air emboli (CAE) and adverse neurologic outcome after CPB.[3,5-7]

With the view to provide neuroprotection during CPB, a generally accepted definition of optimal mean arterial pressure (MAP) to ensure adequate tissue perfusion has not been established. Although cerebral perfusion is assumed to remain constant over a wide range of MAPs, it is generally regulated by MAP rather than the pump flow rate during CPB.[8,9] In the presence of pathologic CAE impairing tissue perfusion, maintaining higher MAP on CPB has the theoretic advantage of enhancing collateral blood flow and facilitating emboli clearance. Yet, this may also lead to cerebral edema or increased delivery of embolic load to the brain.[2,8] In conjunction, the results of the limited observational clinical studies are contradictory, and no comprehensive data exist regarding the contribution of MAP to cerebral outcome after CPB.[10-12]

Therefore, the purpose of the present study was to investigate the influence of MAP during CPB on CAE-induced functional (neurologic and cognitive) and histologic cerebral injury in a randomized and controlled experiment using an established rodent model of CPB combined with CAE.[7]

MATERIALS AND METHODS

The Duke University Institutional Animal Care and Use Committee approved this study, and all procedures met the National Institutes of Health guidelines for animal care (Guide for the Care and Use of Laboratory

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Abbreviations and Acronyms
CAE = cerebral air emboli
CPB = cardiopulmonary bypass
IV = intravenously
MAP = mean arterial pressure
POD = postoperative day
ROI = regions of interest

Animals, available at: www.nap.edu/catalog/5140.html). Thirty male Sprague–Dawley rats (age, 12–14 weeks; weight, 375–400 g; Charles River Laboratories, Inc, Wilmington, Mass) were studied. Animals were randomly assigned to 1 of 3 groups with repetitively administered CAEs (n = 10 each) that differed in the management of MAP during 90 minutes of normothermic CPB. MAP was maintained at 80, 60–70, or 50 mm Hg in the high, standard, and low MAP groups, respectively. MAP was adjusted by varying the inhalational concentration of isoflurane (range, 0.5%–2.5%) or using phenylephrine (not exceeding 2–3 μg intravenously [IV] per bolus).

Surgical Preparation and Cardiopulmonary Bypass

Fasted rats were anesthetized with 5% isoflurane in oxygen in a plastic induction box. After induction of anesthesia, the trachea was intubated and the lungs were mechanically ventilated (Harvard Rodent Respirator; Boston, Mass) with a tidal volume of 10 mL/kg and respiratory rate of 50 to 55 beats/min maintaining arterial P_{CO_2} between 36 and 42 mm Hg. During surgery, anesthesia was maintained with 2.0% to 2.5% isoflurane and fentanyl (25 μg/kg, intravenous, as a bolus injection).

Animals were cannulated for CPB as previously reported.[7,13] Briefly, the tail artery was cannulated for aortic inflow, a multistaged venous return cannula was placed in the heart through the right external jugular vein, and the right superficial caudal epigastric artery was cannulated for monitoring of MAP (model 90603A; SpaceLabs, Inc, Redmond, Wash). After the cannulation of the tail artery, animals received 150 units of heparin. During CPB, anesthesia was maintained using 0.5% to 1.2% isoflurane and fentanyl (150 μg/kg IV). No paralytics were administered until just before CPB when pancuronium (0.1 mg/kg) was administered to prevent spontaneous breathing during CPB. Fentanyl and pancuronium were repeated (at half the dose) at 30-minute intervals, as necessary. Pericranial temperature was monitored with CSC 32 (Omega Engineering, Inc, Stamford, Conn) and maintained at 37.5°C ± 0.1°C using a heating blanket and convective forced-air heating system.

The CPB circuit consisted of a venous reservoir, a peristaltic pump (Tygon; Cole-Patmer Instrument, Vernon Hills, Ill), a membrane oxygenator, and an arterial inflow cannula. An in-line flow probe (2N806 flow probe and T208 volume flowmeter; Transonics Systems, Inc, Ithaca, NY) was used to continuously measure CPB flow. To avoid excessive hemodilution, the bypass circuit was primed with 14 mL whole blood obtained from a heparinized (150 units IV heparin per rat) donor rat. In addition, 6% hetastarch (4 mL) was added to the circuit, as needed. One hundred units of heparin were added to the prime. Arterial line inflow temperature was maintained at 37.5°C using a circulating water bath system. Arterial blood gases were analyzed using a GEM Premier 3000 blood gas/electrolytic analyzer (model 5700; Instrument Laboratories, Inc, Lexington, Mass). Basic physiologic data, including MAP, temperature, and blood gases, were collected 15 minutes before commencement of CPB. All animals were subjected to 90 minutes of normothermic and nonpulsatile CPB with flow rates of 160 to 180 mL/min/kg corresponding to a normal cardiac output in the rat.[12] For the entire CPB period, ventilation of the lungs was discontinued. After 90 minutes of CPB, the animals were weaned from CPB without the need for inotropic support. Heparin-induced anticoagulation was allowed to dissipate spontaneously without supplemental administration of protamine. After decannulation, rats were maintained anesthetized with 0.5% to 1.2% isoflurane, intubated, and ventilated for 1 hour. When adequate spontaneous breathing resumed, the animals were extubated and recovered in an oxygen-enriched box for 24 hours with free access to water and food. During the first 6 hours of recovery, they were continuously observed to identify signs of immediate cerebral death and severe neurologic dysfunction (fixed pupils, absence of spontaneous breathing, seizures, and inability to ambulate). Animals demonstrating signs of severe neurologic dysfunction were sacrificed. All others were returned to their cages and housed individually.

Cerebral Air Embolism

The methodology of the CAE model used in the current study has been reported.[7] Briefly, rats subjected to 90 minutes of normothermic CPB received 10 equally sized CAEs (0.3 μL/single bolus). The choice of 0.3 μL per bolus was based on preliminary work showing that this size of CAE during CPB is associated with a mortality rate of 1% (95% confidence interval, 0.1–14.5) and an incidence for neurologic deficits of 85.8% (95% confidence interval, 40.7–98.2).[7] For the injection of CAEs, a PE-10 catheter (Intramedic; Becton-Dickinson, Sparks, Md) was inserted via the stump of the right external carotid artery and advanced into the right internal carotid artery beyond the pterygopalatine branch (0.8 cm distance) that was ligated. The catheter was connected to a syringe pump (KDS100; KD Scientific Inc, Holliston, Mass). The first embolus was administered at 15 minutes of CPB, and the last embolus was administered at 75 minutes of CPB. By using a Hamilton syringe with a 1.2-cm long needle (5 μL SYR, 75N; Hamilton Co, Reno, Nev), the size of the air bubble could be exactly determined by the placement of the air between 2 μL saline aliquots. After the delivery of the last CAE, 10 μL saline were injected to flush the last air embolus into the cerebral circulation.

Neurologic and Neurocognitive Testing

On the third and seventh postoperative days (PODs), animals underwent standardized functional neurologic testing using an established neurologic scoring system that evaluates 4 different functions, including general status, simple motor deficit, complex motor deficit, and sensory deficit.[14] The score given to each animal at the completion of the testing (by an observer blinded to group assignment) was the sum of all 4 individual scores: 0 was the minimum (best) score and 48 was the maximum (worst) score.

In addition to the neurologic evaluation, neurocognitive outcome was evaluated daily (starting on POD 3) in the Morris water maze using a computerized video tracking system (EthoVision; Noldus, Wageningen, The Netherlands).[15] The Morris water maze consisted of a 1.5-m diameter, 30-cm deep pool of water (27°C) with a hidden submerged (3 cm below surface) platform in 1 quadrant. Rats were placed in the water in a dimly lit room with various visual clues around the maze. The time to locate the submerged platform (defined as the latency) was measured to test for impairment in visuospatial learning and memory components of neurocognition. Rats underwent daily testing in the water maze with 4 trials per testing period, each limited to a 90-second water exposure. Each of the trials was begun from a separate quadrant. Testing was performed for 5 consecutive days until POD 7.

Histologic Examination

After completion of the testing on the final day, the animals were anesthetized with 5% isoflurane and decapitated. The brains were removed, snap-frozen at –40°C in 2-methyl-butane, and stored at –80°C for later analysis.

Infarct volume was measured by using previously published methods.[14] Serial quadruplicate 20-μm–thick coronal sections were taken by using a cryotome at 660-μm intervals over the rostrocaudal extent of the infarct. The sections were dried and stained with hematoxylin–eosin. A representative section from each 660-μm interval was digitized with a video camera controlled by an image analyzer (M2 Turnkey System; Imaging Research,

St Catharines, Ontario, Canada). The following regions of interest (ROI) were cursor-outlined: noninfarcted ipsilateral cerebral cortex, noninfarcted ipsilateral subcortex, contralateral cerebral cortex, and contralateral subcortex. The area within each ROI (square millimeters) was determined by automated counting of the calibrated pixels contained within the ROI. Ipsilateral noninfarcted cortex and subcortex areas were subtracted from the corresponding contralateral ROI values. Infarct volumes (cubic millimeters) were computed as running sums of subtracted infarct area multiplied by the known interval (eg, 660 μm) between sections over the rostrocaudal extent of the infarct calculated as an orthogonal projection. The number of infarct areas was also counted.

Statistical Analysis

Statistical analyses were performed using SPSS 12.0 (SPSS Inc, Chicago, Ill). All data are expressed as mean ± standard deviation. Data among the groups were compared using chi-square test, Fisher's exact test, or 1-way analysis of variance followed by post hoc Bonferroni test as appropriate. Data within the group were compared using paired *t* test or repeated-measures analysis of variance followed by post hoc Dunnett's test as appropriate.

RESULTS

Physiologic Parameters

Table 1 displays the physiologic variables of rats treated with high, standard, and low MAP during CPB combined with CAE. In intergroup comparisons, hemoglobin and glucose concentrations, pH, $Paco_2$, and pericranial temperature were statistically different at various time points of measurements; however, all within normal limits.

Neurologic Outcome

In intergroup comparisons, neurologic scores were better in the high and standard MAP group compared with the low MAP group at both POD 3 (7.1 ± 5.6, $P = .0183$; 5.4 ± 2.6, $P = .0025$; and 12.2 ± 4.8 in the high, standard, and low MAP groups, respectively) and POD 7 (4.8 ± 4.1, $P = .0287$; 4.6 ± 2.0, $P = .0217$; and 9.2 ± 5.8 in the high, standard, and low MAP groups, respectively; Figure 1). In intragroup comparisons, neurologic scores in all of the 3 groups were significantly improved on POD 7 compared with POD 3 ($P = .041$, $P < .001$, and $P = .021$ in the high, standard, and low MAP groups, respectively).

Cognitive Outcome

In intergroup comparisons of the water maze latencies, denoting the cumulative time taken by animals to find the platform based on the 4 trials of each day, animals in the

TABLE 1. Physiologic parameters

Parameters	Baseline	CPB 30 min	CPB 60 min	CPB 90 min	After CPB 60 min
MAP (mm Hg)					
High MAP	62 ± 6	82 ± 12†	84 ± 7	87 ± 7	82 ± 6
Standard MAP	56 ± 5*,†	56 ± 4*	59 ± 5*,†	63 ± 5*,†	79 ± 11
Low MAP	65 ± 8	50 ± 2	49 ± 5*	50 ± 4*	76 ± 10
Hemoglobin (mg/dL)					
High MAP	12.3 ± 0.8	10.2 ± 0.7	10.7 ± 0.6	11.0 ± 0.6	10.6 ± 0.5
Standard MAP	11.5 ± 1.2	9.7 ± 0.5	9.7 ± 0.6	10.0 ± 0.6*	10.9 ± 1.3
Low MAP	12.1 ± 0.6	9.7 ± 0.6	9.9 ± 0.6	10.0 ± 0.7*	10.3 ± 0.9
Glucose (mg/dL)					
High MAP	123 ± 31	120 ± 21			111 ± 24
Standard MAP	114 ± 18	111 ± 9†			88 ± 15†
Low MAP	126 ± 24	129 ± 22			112 ± 34
pHa					
High MAP	7.47 ± 0.05	7.42 ± 0.12	7.39 ± 0.03	7.38 ± 0.04	7.37 ± 0.10
Standard MAP	7.46 ± 0.07	7.43 ± 0.04	7.43 ± 0.04*	7.43 ± 0.05*,†	7.40 ± 0.04
Low MAP	7.47 ± 0.05	7.40 ± 0.02	7.41 ± 0.03	7.38 ± 0.04	7.37 ± 0.10
Pao_2 (mm Hg)					
High MAP	181 ± 35	454 ± 57	473 ± 67	474 ± 48	309 ± 104
Standard MAP	173 ± 49	450 ± 40	463 ± 108	467 ± 102	252 ± 113
Low MAP	155 ± 52	454 ± 57	469 ± 41	459 ± 125	253 ± 97
$Paco_2$ (mm Hg)					
High MAP	34 ± 4	41 ± 4	41 ± 4	40 ± 4	40 ± 9
Standard MAP	36 ± 8	38 ± 3†	39 ± 3	39 ± 4	39 ± 6
Low MAP	35 ± 3	41 ± 2	40 ± 2	39 ± 4	38 ± 4
Pericranial temperature (°C)					
High MAP	37.0 ± 0.8	37.1 ± 0.6	37.4 ± 0.3	37.5 ± 0.2	37.5 ± 0.5
Standard MAP	36.8 ± 0.6	36.5 ± 0.5*	37.0 ± 0.5*,†	37.3 ± 0.2	37.7 ± 0.4
Low MAP	36.9 ± 0.5	36.6 ± 0.7	37.4 ± 0.3	37.3 ± 0.4	37.7 ± 0.5

CPB, Cardiopulmonary bypass; *MAP,* mean arterial pressure; *Pao_2,* arterial oxygen tension; *$Paco_2$,* arterial carbon dioxide tension. Values are mean ± standard deviation. Each group consists of 10 rats. *$P < .05$ compared with high MAP group. †$P < .05$ compared with low MAP group.

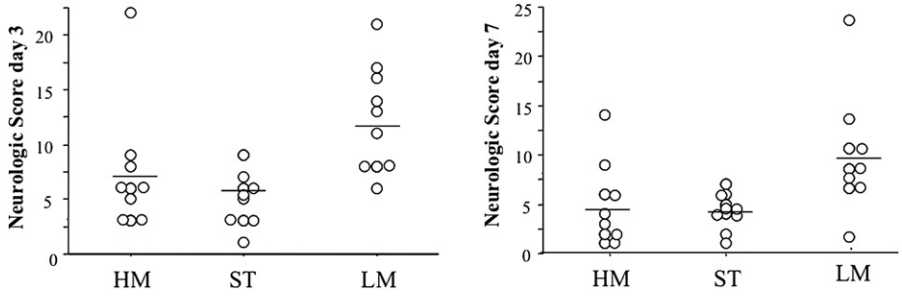

FIGURE 1. Neurologic function was evaluated on PODs 3 and 7 using a protocol that included assays of general status, vertical screen climbing, balance beam, and sensory performance (total possible deficit points = 48, 0 = no deficit). Animals exposed to MAP of 80 mm Hg *(HM)* or 60 to 70 mm Hg *(ST)* during normothermic CPB combined with CAE demonstrated significantly lower neurologic score on both PODs 3 and 7 compared with those exposed to MAP of 50 mm Hg (*LM*). *HM,* High MAP; *ST,* standard MAP; *LM,* low MAP.

standard MAP group had shorter latencies compared with the high MAP group at POD 3 ($P = .019$; Table 2). Latencies were significantly shorter in the high MAP group compared with the standard MAP group on POD 6 ($P = .0327$) and POD 7 ($P = .0271$). Latency in the high MAP group also demonstrated a trend toward being shorter compared with the low MAP group on POD 6 ($P = .0852$). In intragroup comparisons, latencies were improved in the high MAP group on PODs 4 to 7 compared with the baseline value on POD 3 (all $P < .001$). Latency was also improved in the low MAP group on PODs 5 ($P = .049$), 6 ($P = .044$), and 7 ($P = .014$) compared with the baseline value on POD 3, whereas it remained similar in the standard MAP group throughout. There were no intergroup or intragroup differences in swimming speeds at all time points of measurements (Table 2).

Histology

No differences were found between groups with respect to total infarction volume (Figure 2). The number of infarct areas was also similar among the groups (1.3 ± 0.7, 0.8 ± 0.6, 1.2 ± 0.9 in the high, standard, and low MAP groups, respectively, $P = .106$)

DISCUSSION

The current study provides primary evidence that using a higher MAP during CPB improved postoperative functional neurologic and neurocognitive outcome induced by CAE and CPB. These functional benefits, however, could not be extended to a reduced cerebral infarct volume.

In addition to the less frequent overt manifestation of cerebral injury stroke, neurocognitive decline is a well-recognized complication after cardiac surgery with high prevalence and persistence leading to long-term consequences mandating the need for strategies aimed at reducing its occurrence.[16] Among the complex and multifactorial causes, the principal cause of neurocognitive dysfunction is considered to be cerebral microembolic load during CPB.[2,3] Cerebral microemboli occur in virtually all patients undergoing CPB with the majority being gaseous.[4,5] Clinically, cerebral emboli during CPB were associated with impaired memory and demonstrated to be a significant predictor of neuropsychologic dysfunction.[3,5,6] Moreover, a recent study in a similar rat model of CPB demonstrated the relationship between CAE and postoperative cerebral injury.[7] In that study, total cerebral infarction volume induced by air emboli correlated with postoperative neurologic function, confirming the role of CAE during normothermic CPB on postoperative neurologic and neurocognitive dysfunction.

In view of neuroprotective strategies in the setting of acute ischemic stroke as caused by CAE during CPB, none of the pharmacologic agents developed to interrupt biochemical mechanisms leading to neuronal death demonstrated clinical success.[17] Thus, the importance of collateral

TABLE 2. Morris water maze test

	Day 3	Day 4	Day 5	Day 6	Day 7
Latencies (s)					
High MAP	260 ± 59	108 ± 37†	70 ± 55†	39 ± 24†	36 ± 29†
Standard MAP	178 ± 81*	155 ± 109	131 ± 102	126 ± 107*	126 ± 123*
Low MAP	243 ± 77	150 ± 108	111 ± 116†	110 ± 108*,†	91 ± 82†
Swimming speed (cm/min)					
High MAP	22.6 ± 2.2	24.4 ± 3.8	26.7 ± 5.3	26.2 ± 4.6	23.6 ± 5.6
Standard MAP	20.6 ± 3.0	24.6 ± 6.6	23.1 ± 4.6	22.1 ± 5.8	26.4 ± 4.8
Low MAP	21.6 ± 4.1	24.4 ± 5.6	23.9 ± 4.1	26.4 ± 6.6	25.4 ± 5.3

MAP, Mean arterial pressure. Values are mean ± standard deviation. *$P < .05$ compared with high MAP group. †$P < .05$ compared with baseline value in each group.

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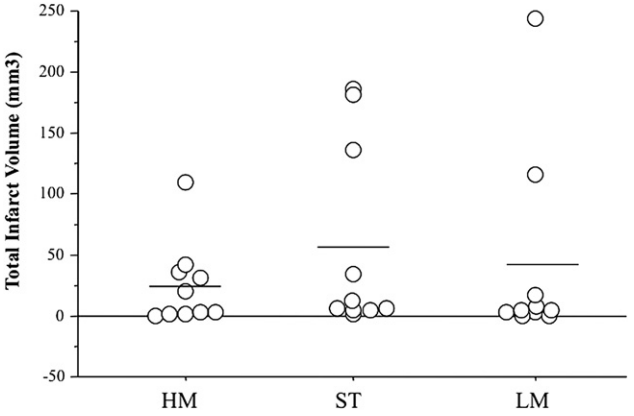

FIGURE 2. Histologic outcome 7 day after normothermic CPB combined with CAE was evaluated by cerebral infarction volume. No statistically significant differences were noted in respect to the different MAP management (80 mm Hg, 60–70 mm Hg, and 50 mm Hg in the HM, ST, and LM groups, respectively) during CPB. *HM,* High MAP; *ST,* standard MAP; *LM,* low MAP.

therapeutics aimed at treating the salvageable ischemic penumbra is being increasingly emphasized, which can be achieved by deliberate elevation of blood pressure to promote collateral circulation.[17,18] Higher MAP during CPB may also facilitate emboli clearance. On the other hand, higher MAP during CPB may paradoxically increase the delivery of embolic load to the brain and promote hyperemia and cerebral edema formation.[2,8,19] In conjunction, clinical studies addressing the relationship between MAP during CPB and neurologic outcome demonstrated conflicting results.[10-12] Most of the studies are retrospective reviews depicting the relationship between lower MAP and adverse cerebral outcome. The only existing randomized clinical trial revealed better combined cardiac and neurologic outcome in the higher MAP group, although there was not a statistically significant difference in these outcomes when examined individually.[12] Moreover, the average MAP in the high pressure group was actually significantly lower than their targeted pressure. As the results of the current study indicate, using higher MAP during CPB in the presence of CAE was consistently associated with improved overall neurologic score and shorter latencies in water maze compared with lower MAP. Although standard MAP resulted in better neurologic score than lower MAP, it was associated with longer latencies in water maze compared with the high MAP group. The neurologic scoring system was derived to evaluate 4 different functions (general status, simple motor deficit, complex motor deficit, and sensory deficit) by combining elements from several previously described scoring systems. Lesions in distinct brain regions, such as the hippocampus, striatum, basal forebrain, cerebellum, and cerebral cortex, have been demonstrated to impair performance in the Morris water maze. The test measures the latency to find a submerged platform within the maze, which serves as a surrogate of impairment in visuospatial learning and memory components of neurocognition.[15] Therefore, the current study clearly depicts improved functional neurologic and neurocognitive outcome after CAE and CPB by using higher MAP during CPB. These functional benefits, however, were not accompanied by reduced cerebral infarct volume. The main potential advantage of using higher MAP in regional ischemia would be to increase collateral flow to the viable penumbral regions adjacent to areas embolized during cardiac surgery, which would lead to decreased infarct volume. In our study, however, although the high MAP group had the lowest infarct volume, this was not statistically significant. The discordance between function and histology in this present study is, however, in agreement with the findings of previous regional ischemia models in which infarct size often poorly correlates with functional outcome.[20,21] This discrepancy may be attributable to the ability of air bubbles to not only occlude small arterioles and cause distal ischemia but also to activate inflammatory cascade exacerbating the ischemic insult, which was not assessed in this study, because higher MAP may facilitate the clearance of emboli as well.[22,23] Although cerebral perfusion is assumed to be constant over a wide range of MAPs, substantial variability exists at the lower limit of cerebral autoregulation, with some studies reporting the lower limit at the range of 73 to 88 mm Hg.[2,8] Moreover, embolism itself caused regional impairment of cerebral autoregulation in a dog model of CPB supporting the dominant role of perfusion pressure on cerebral blood flow potentially affecting the fate of the delivered air emboli.[24] The histologic findings of the current study demonstrate that the infarct volume and especially the number of infarcted areas were similar among groups. Because the flow rate during CPB was maintained constant, this implies that using higher MAP at least does not result in an increased embolic load to the brain and standard or even lower MAP during CPB is not advantageous in terms of reduced embolic load delivery.

To delineate the effects of various MAP on neurologic outcome after CPB with minimal confounders, we used a well-established animal model of cerebral injury induced by CAE during CPB, which enables long-term follow-up and assessment.[7] However, even the most sophisticated animal models will likely fail to simulate the clinical situation completely, and several limitations should be acknowledged. These include the health characteristics of animals because the rats that were studied were healthy, whereas humans who undergo CPB often have other comorbidities affecting the cerebral vasculature. Also, species difference regarding the susceptibility to ischemia–reperfusion-induced neurologic injury should be taken into consideration. Limitations inherent to the current rat model of CPB combined with CAE are as follows. Because of

technical limitations and miniaturization of this model, only 10 equally sized CAEs were administered. Also, to allow long-term survival, median sternotomy, direct cardiac cannulation, and opening of cardiac cavities were not performed. Thus, generation of a shower of CAEs as detected during CPB in the clinical setting could not be obtained, although the embolus size (0.3 μL) and the delivery method were selected to generate neurologic deficit in the majority of rats without mortality and to ensure standardized and controlled CAE.[7]

CONCLUSIONS

The use of higher MAP during CPB in this rat model of CAE conveyed beneficial effects on functional cerebral outcome. The use of lower MAP was associated with poor functional neurologic outcome and seems to have no advantage in terms of decreased delivery of embolic load to the central nervous system. Maintaining higher perfusion pressures in situations of increased cerebral embolic load during CPB may be considered as a collateral therapeutic strategy.

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