Cases(1)/Controls(0)= 1					Cases(1)/Controls(0)= 0				
	Established risk factors + new risk factors					Established risk factors + new risk factors			
	1:<0.1	2:0.1-0.2	3:0.2-0.3	4:>=0.2		1:<0.1	2:0.1-0.2	3:0.2-0.3	4:>=0.2
	N	N	N	N		N	N	N	N
Established risk factors					Established risk factors				
1:<0.1	621	43	1	- 6	1:<0.1	68147	363	2	
2:0.1-0.2	39	228	69	3	2:0.1-0.2	417	1280	214	8
3:0.2-0.3		59	140	66	3:0.2-0.3	2	221	365	142
4:>=0.2		3	52	177	4:>=0.2		7	135	268

Fig. 1. Reclassification tables. If the larger model (which includes the Surgical Apgar Score) on average assigns a higher risk class to cases and a lower risk class to noncases than the small model (no Surgical Apgar Score), then net reclassification index is positive.

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Competing Interests

The authors declare no competing interests.

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References

- Terekhov MA, Ehrenfeld JM, Wanderer JP: Preoperative surgical risk predictions are not meaningfully improved by including the Surgical Apgar Score: An analysis of the risk quantification index and present-on-admission risk models.
 ANESTHESIOLOGY 2015; 123:1059–66
- Hyder JA, Kor DJ, Cima RR, Subramanian A: How to improve the performance of intraoperative risk models: An example with vital signs using the surgical appar score. Anesth Analg 2013: 117:1338-46
- 3. Pencina MJ, D'Agostino RB Sr, D'Agostino RB Jr, Vasan RS: Evaluating the added predictive ability of a new marker: From area under the ROC curve to reclassification and beyond. Stat Med 2008; 27:157–72; discussion 207–12

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Arterial Pressure and Cardiopulmonary Bypass

To the Editor:

I was pleased to see our work cited in the recent Review Article, "Cardiac Output and Cerebral Blood Flow: The Integrated Regulation of Brain Perfusion in Adult Humans." 1,2 Nevertheless, some conclusions made by the authors may have been misleading. They state that during cardiopulmonary bypass, alpha-stat management

of carbon dioxide resulted in cerebral blood flow correlated with arterial blood pressure, whereas pH-stat management resulted in cerebral blood flow correlated with pump flow. Yet, clinical and laboratory evidence indicates that this explanation may be deficient. When Rogers et al.3 directly addressed this issue in a study of cardiac patients randomly assigned to either alpha-stat or pH-stat management, both groups showed cerebral blood flow dependent on arterial blood pressure and not dependent on cardiopulmonary bypass flow rate. Furthermore, Hindman et al.4 demonstrated that in pH-stat-managed rabbits, during constant-flow cardiopulmonary bypass, increases in arterial blood pressure resulted in large increases in cerebral blood flow. Meng et al.2 also state that during cardiopulmonary bypass, organ perfusion is propelled by centrifugal pump. However, in several studies they cite, cardiopulmonary bypass was by roller pump.^{5–7}

Competing Interests

The author declares no competing interests.

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References

- Schwartz AE, Sandhu AA, Kaplon RJ, Young WL, Jonassen AE, Adams DC, Edwards NM, Sistino JJ, Kwiatkowski P, Michler RE: Cerebral blood flow is determined by arterial pressure and not cardiopulmonary bypass flow rate. Ann Thorac Surg 1995; 60:165–9; discussion 169–70
- Meng L, Hou W, Chui J, Han R, Gelb AW: Cardiac output and cerebral blood flow: The integrated regulation of brain perfusion in adult humans. Anesthesiology 2015; 123:1198–208
- 3. Rogers AT, Prough DS, Roy RC, Gravlee GP, Stump DA, Cordell AR, Phipps J, Taylor CL: Cerebrovascular and cerebral metabolic effects of alterations in perfusion flow rate during hypothermic cardiopulmonary bypass in man. J Thorac Cardiovasc Surg 1992; 103:363–8
- Hindman BJ, Dexter F, Cutkomp J, Smith T: pH-stat management reduces the cerebral metabolic rate for oxygen during profound hypothermia (17 degrees C). A study during cardiopulmonary bypass in rabbits. Anesthesiology 1995; 82:983–95; discussion 24A

- Schell RM, Kern FH, Greeley WJ, Schulman SR, Frasco PE, Croughwell ND, Newman M, Reves JG: Cerebral blood flow and metabolism during cardiopulmonary bypass. Anesth Analg 1993; 76:849–65
- Soma Y, Hirotani T, Yozu R, Onoguchi K, Misumi T, Kawada K, Inoue T: A clinical study of cerebral circulation during extracorporeal circulation. J Thorac Cardiovasc Surg 1989; 97:187–93
- Tokunaga S, Imaizumi T, Fukae K, Nakashima A, Hisahara M, Tominaga R, Takeshita A, Yasui H, Tokunaga K: Effects of hypothermia during cardiopulmonary bypass and circulatory arrest on sympathetic nerve activity in rabbits. Cardiovasc Res 1996; 31:769–76

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In Reply:

We welcome Dr. Schwartz's interest in our article. However, his comments are misleading in relation to cardiac output and cerebral blood flow (CBF) during cardiopulmonary bypass.

Interpretation of data from the relatively small body of literature on the relationship among blood pressure, cardiac output/pump flow, and CBF is confounded by different experimental conditions, species, and CBF measurement methods. Furthermore, hypercarbia (in pH-stat management) and profound hypothermia can cause cerebral vasoplegia, resulting in pressure dependency. We assume that when Dr. Schwartz states that our "explanation is deficient," he is referring to the discrepancies in the literature that likely stem from these confounders.

With alpha-stat management, CBF was shown to correlate with blood pressure, not with pump flow.² This fact is supported by Dr. Schwartz's own study. With pHstat management, Soma et al.,3 whose study was cited by Dr. Schwartz as well as us, demonstrated that CBF is correlated with pump flow and not with blood pressure in humans. However, this has not been a consistent finding, perhaps reflecting the confounders mentioned. Rogers et al., 4 cited by Dr. Schwartz, performed a study in patients randomized to alpha-stat or pH-stat in which the primary aim of the study was to investigate the changes in CBF at two-pump flow rates applied in random order while maintaining a constant blood pressure. Their conclusion was that pump flow exerts no effect on CBF with either management strategy. They did not mention that CBF was dependent on blood pressure because it was kept constant. Hindman et al.5 investigated the effect of pH management (alpha- or

pH-stat) on cerebral metabolic rate of oxygen during profound hypothermia (17°C) in rabbits. There was an imbalance in blood pressures in the two groups (alpha- or pH-stat), requiring them to perform a substudy to normalize the blood pressure for comparison of cerebral metabolic rate of oxygen. The finding of large changes in CBF by blood pressure was incidental and was likely confounded by the profound hypothermia.

Our assertion, "Organ perfusion is propelled by centrifugal pump," is a general statement to describe the physiology of patients on cardiopulmonary bypass. Roller pumps are no longer used in most adult surgical centers. The "centrifugal pump" did not refer to any quoted studies in the article. In addition, evidence suggests that centrifugal pump and roller pump have little influence on CBF during cardiopulmonary bypass.⁶

Competing Interests

The authors declare no competing interests.

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References

- Meng L, Hou W, Chui J, Han R, Gelb AW: Cardiac output and cerebral blood flow: The integrated regulation of brain perfusion in adult humans. Anesthesiology 2015; 123:1198–208
- 2. Schwartz AE, Sandhu AA, Kaplon RJ, Young WL, Jonassen AE, Adams DC, Edwards NM, Sistino JJ, Kwiatkowski P, Michler RE: Cerebral blood flow is determined by arterial pressure and not cardiopulmonary bypass flow rate. Ann Thorac Surg 1995; 60:165–9; discussion 169–70
- Soma Y, Hirotani T, Yozu R, Onoguchi K, Misumi T, Kawada K, Inoue T: A clinical study of cerebral circulation during extracorporeal circulation. J Thorac Cardiovasc Surg 1989; 97:187–93
- Rogers AT, Prough DS, Roy RC, Gravlee GP, Stump DA, Cordell AR, Phipps J, Taylor CL: Cerebrovascular and cerebral metabolic effects of alterations in perfusion flow rate during hypothermic cardiopulmonary bypass in man. J Thorac Cardiovasc Surg 1992; 103:363–8
- Hindman BJ, Dexter F, Cutkomp J, Smith T: pH-stat management reduces the cerebral metabolic rate for oxygen during profound hypothermia (17 degrees C): A study during cardiopulmonary bypass in rabbits. Anesthesiology 1995; 82:983–95; discussion 24A
- Hindman BJ, Dexter F, Smith T, Cutkomp J: Pulsatile versus nonpulsatile flow: No difference in cerebral blood flow or metabolism during normothermic cardiopulmonary bypass in rabbits. Anesthesiology 1995; 82:241–50

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