Cardiology in the Young

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Impact of the superior cavopulmonary anastomosis on cerebral oxygenation

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Brief Report

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Abstract

Background: Patients with univentricular heart disease may undergo a superior cavopulmonary anastomosis, an operative intervention that raises cerebral venous pressure and impedance to cerebral venous return. The ability of infantile cerebral autoregulation to compensate for this is not well understood. *Materials and methods:* We identified all patients undergoing a superior cavopulmonary anastomosis (cases) and compared metrics of cerebral oxygenation upon admission to the ICU with patients following repair of tetralogy of Fallot or arterial switch operation (controls). The primary endpoint was cerebral venous oxyhaemoglobin saturation measured from an internal jugular venous catheter. Other predictor variables included case–control assignment, age, weight, sex, ischemic times, arterial oxyhaemoglobin saturation, mean arterial blood pressure, and superior caval pressure. *Results:* A total of 151 cases and 350 controls were identified. The first post-operative cerebral venous oxyhaemoglobin saturation was significantly lower following superior cavopulmonary anastomosis than in controls (44 ± 12 versus $59 \pm 15\%$, $p < 0.001$), as was arterial oxyhaemoglobin saturation (81 ± 9 versus $98 \pm 5\%$, $p < 0.001$). Cerebral venous oxyhaemoglobin saturation correlated poorly with superior caval pressure in both groups. When estimated by linear mixed effects model, arterial oxyhaemoglobin saturation was the primary determinant of central venous oxyhaemoglobin saturation in both groups ($\beta = 0.79$, $p = 3 \times 10^{-14}$); for every 1% point increase in arterial oxyhaemoglobin saturation, there was a 0.79% point increase in venous oxyhaemoglobin saturation. In this model, no other predictors were significant, including superior caval pressure and case–control assignment. *Conclusion:* Cerebral autoregulation appears to remain intact despite acute imposition of cerebral venous hypertension following superior cavopulmonary anastomosis. Following superior cavopulmonary anastomosis, cerebral venous oxyhaemoglobin saturation is primarily determined by arterial oxyhaemoglobin saturation.

Children with successful initial palliation of univentricular heart disease often undergo a superior cavopulmonary anastomosis in infancy. In this circulation, impedance to cerebral venous drainage is acutely increased as the resistance in the pulmonary circuit interrupts cerebral venous drainage into the atrium. Studies have demonstrated that cerebral near-infrared spectroscopy values are similar prior to and following superior cavopulmonary anastomosis.[1,2] However, this technique has been shown to be insensitive to detecting cerebral hypoxia in cyanotic patients.[3,4] The purpose of this study was to compare a direct measure of cerebral oxygenation – cerebral venous oxyhaemoglobin saturation – between a large cohort of patients undergoing superior cavopulmonary anastomosis with those undergoing other major congenital heart operations within the first year of life.

Materials and methods

Following institutional review board approval (IRB-P00027939, exempt from informed consent), we retrospectively compared metrics of cerebral oxygenation in the acute post-operative period between children undergoing superior cavopulmonary anastomosis (cases) and children undergoing repair of tetralogy of Fallot repair or an arterial switch operation (taken together as a control group) between 1 January, 2009 and 31 December, 2018 at our institution. It is routine practice at our institution that nearly every patient undergoing a superior cavopulmonary anastomosis returns to the ICU intubated with an internal jugular venous catheter in place for monitoring. We excluded patients on extracorporeal membrane oxygenator support and those extubated prior to recording of the following endpoints in the ICU. Endpoints included the first post-operative arterial oxyhaemoglobin saturation, central venous oxyhaemoglobin saturation, and superior caval pressure measured from a right internal jugular venous line, atrial pressure, mean arterial blood pressure, and haemoglobin level. Calculated variables included arteriovenous oxyhaemoglobin saturation difference and cerebral perfusion pressure (mean arterial blood pressure − superior caval pressure). Demographic variables noted were age, sex, weight, and cardiopulmonary bypass time. The relationship between cerebral venous oxyhaemoglobin

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saturation and arterial oxyhaemoglobin saturation or superior caval pressure was determined by linear regression analysis by group (GraphPad Prism v 7.0 d, GraphPad Software, La Jolla, CA, USA). In order to identify the determinants of cerebral venous oxyhaemoglobin saturation, we created a linear model of this endpoint that was refined by stepwise selection using Akaike information criteria (R version 3.4.3 R Core Team, 2019.). Predictors included arterial oxyhaemoglobin saturation, arterial blood pressure, superior caval pressure, atrial pressure, haemoglobin, ischemic times, and demographic variables.

Results

A total of 151 cases and 350 controls were identified to meet inclusion and avoid exclusion criteria. Compared with controls, patients undergoing superior cavopulmonary anastomosis had significantly higher age (5.4 ± 1.7 versus 2.3 ± 2.6 months, $p < 0.001$) and weight (6.0 ± 1.1 versus 4.3 ± 1.6 kg, $p < 0.001$), though haemoglobin concentration was similar (13.7 ± 1.7 versus 13.6 ± 2.0 g/dl, $p = 0.77$). Cardiopulmonary bypass time was significantly shorter in superior cavopulmonary anastomosis than in controls (118 ± 52 versus 152 ± 51 minutes, $p < 0.001$).

The first post-operative cerebral venous oxyhaemoglobin saturation was significantly lower following superior cavopulmonary anastomosis than in controls (44 ± 12 versus 59 ± 15%, $p < 0.001$), as was arterial oxyhaemoglobin saturation (81 ± 9 versus 98 ± 5%, $p < 0.001$). The arteriovenous oxyhaemoglobin saturation difference was similar between groups (36 ± 10 versus 38 ± 15%, $p = 0.09$), as was the slope of the relationship between arterial and venous oxyhaemoglobin saturation (slope 0.8 (95% confidence interval, 0.6–1.0) versus 1.0 (0.7–1.3), $p = 0.26$, linear regression, Fig 1a). Following superior cavopulmonary anastomosis, superior caval pressure was significantly higher (16 ± 4 versus 10 ± 4 mmHg, $p < 0.001$) and cerebral perfusion pressure was significantly lower (49 ± 10 versus 55 ± 14 mmHg, $p < 0.001$). Cerebral venous oxyhaemoglobin saturation correlated poorly with superior caval pressure in both groups (Fig 1b). When estimated by linear mixed effects model, arterial oxyhaemoglobin saturation was the primary determinant of cerebral venous oxyhaemoglobin saturation in both groups ($\beta = 0.79$, $p = 2 \times 10^{-16}$); for every 1% point decrease in arterial oxyhaemoglobin saturation, there was a 0.79% point decrease in venous oxyhaemoglobin saturation. In this model, no other predictors were significant (supplementary results), though the model only accounted for 32% of the variability. Specifically, patient group assignment (i.e. cavopulmonary anastomosis versus not) was not a significant contributor to cerebral venous oxyhaemoglobin saturation, nor was cerebral perfusion pressure, central venous pressure, or haemoglobin.

Discussion

We show that the presence of a cavopulmonary anastomosis is not an independent contributor to cerebral venous oxyhaemoglobin saturation when arterial oxyhaemoglobin saturation is accounted for. The fact that neither superior caval pressure nor cerebral perfusion pressure was significant determinants of cerebral venous oxyhaemoglobin saturation, despite an acute rise in the venous pressure and acute fall in the perfusion pressure, suggests that cerebral autoregulation was well preserved in the cohort we studied. Said another way, if a patient undergoing tetralogy of Fallot repair exhibits the same arterial oxyhaemoglobin saturation as another patient following a superior cavopulmonary anastomosis, they would be expected to have a similar cerebral venous oxyhaemoglobin saturation despite the differences in venous pressures.

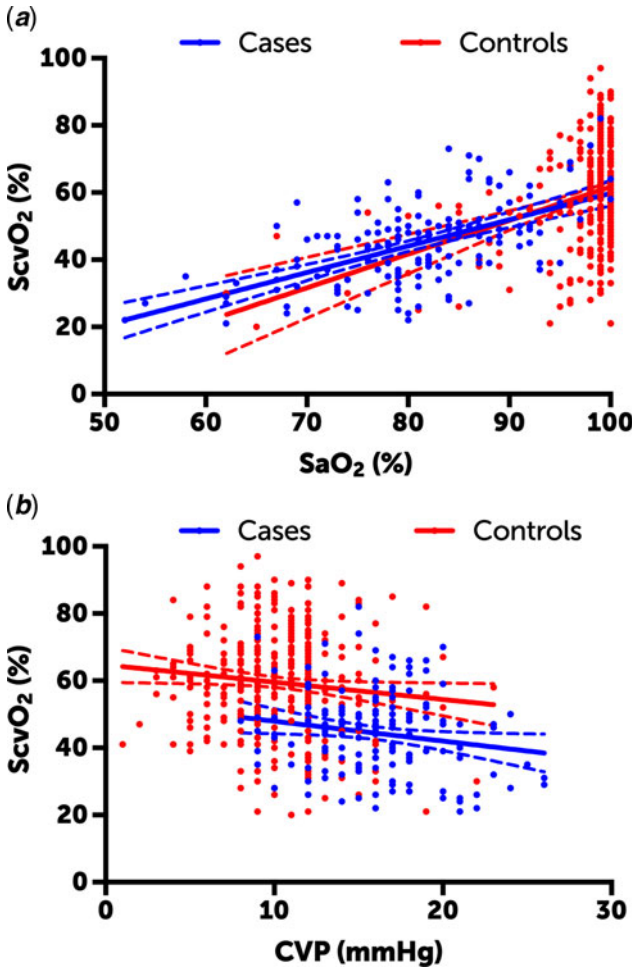

Figure 1. (***a***) Scatter plot and linear regression analyses of the first post-operative $ScvO_2$ and its correlation with first post-operative SaO_2 ($r^2 = 0.33$). Slope of the relationship between $ScvO_2$ and SaO_2 is similar between cases [red, 0.78 (95% confidence interval 0.61, 0.96)] and controls [blue, 1.00 (0.68, 1.32); $p = 0.26$]. (***b***) First post-operative $ScvO_2$ correlated poorly with first post-operative CVP ($r^2 = 0.03$). Slope of the relationship between $ScvO_2$ and CVP is similar between cases [red, 0.78 (95% confidence interval 0.61, 0.96)] and controls [blue, 1.00 (0.68, 1.32); $p = 0.85$]. For (***a***) and (***b***), data are individual patients, lines are linear regression line, error = 95% confidence interval of linear regression line. $ScvO_2$ = central venous oxyhaemoglobin saturation; SaO_2 = arterial oxyhaemoglobin saturation; CVP = central venous pressure.

This finding is not intuitive given that cerebral autoregulation may be impaired in a number of settings, including following cardiac arrest or general anaesthesia.[5,6] Prior studies examining this question have had small sample sizes and utilised near-infrared spectroscopy[1,2] which has been shown to be insensitive in detecting cerebral hypoxia in cyanotic patients.[3,4] Our institutional practice of placing an internal jugular venous catheter in nearly all post-operative congenital heart surgery patients provides a direct window into cerebral oxygenation. Although we did not find that haemoglobin concentration was a significant predictor of central venous oxyhaemoglobin saturation, we were underpowered to detect the impact of this due to the relatively narrow range of haemoglobin (i.e. lack of significant anaemia) in the early post-operative period.

We also found that amongst the variables we examined, arterial hypoxia explains the majority of cerebral hypoxia and that the

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superior cavopulmonary anastomosis with its attendant cerebral venous hypertension does not additively contribute to cerebral hypoxia, with the caveat that patients in this cohort were selected for this procedure based on a low pulmonary vascular resistance. These findings highlight the importance of manoeuvres to diminish arterial hypoxaemia (e.g. providing supplemental oxygen and optimising pulmonary mechanics) to minimise cerebral hypoxia. An important limitation of this study is that it includes assessment of cerebral oxygenation at a single time point in intubated and sedated patients; we are therefore unable to comment on the effects of extubation and wakefulness on cerebral oxygen demand and supply following the Glenn procedure. As noted previously, our model accounted for only 32% of variability in superior caval oxyhaemoglobin saturation; thus, other variables likely contribute significantly to cerebral oxygenation, including arterial and tissue PO_2, arterial partial pressure of carbon dioxide ($PaCO_2$), the precise location of the internal jugular catheter, and differences in anaesthetic state (and therefore cerebral metabolic rate) at the time of sampling, and likely others.

Conclusion

Cerebral autoregulation appears to remain intact despite acute imposition of cerebral venous hypertension following superior cavopulmonary anastomosis. Following superior cavopulmonary anastomosis, cerebral venous oxyhaemoglobin saturation is primarily determined by arterial oxyhaemoglobin saturation.

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Author Contributions. Mr Lingyu Zhou performed statistical analysis and edited the manuscript. Dr Nikhil Thatte collected the primary data, performed data analysis, and wrote the manuscript. Dr John N. Kheir oversaw all aspects of the work, including data collection, data analysis, data interpretation, and edited the manuscript.

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Conflicts of Interest. None.

Ethical Standards. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guidelines on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008, and has been approved by the Boston Children's Hospital Institutional Review Board.

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