The Royal Society of Medicine

Journal of the Royal Society of Medicine; 2019, Vol. 112(12) 512–513
DOI: 10.1177/0141076819877551

Surgery for Eisenmenger syndrome: time for a rethink?

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Traditional teaching is that corrective surgery is contraindicated in established Eisenmenger syndrome. Developments in surgical techniques and better understanding of the physiology may mean that surgery has a role.

Longstanding congenital heart defects associated with a systemic-to-pulmonary shunt can cause severe pulmonary arterial hypertension: right-sided cardiac pressures can approach, equal or even exceed left-sided pressures[1,2] which eventually leads to partial or complete shunt reversal (from left-to-right to bidirectional or right-to-left), with cyanosis from desaturated blood in the systemic circulation. This is Eisenmenger syndrome. Left uncorrected, 50% of ventricular septal defects, 10% of atrial septal defects and virtually all persistent ductus cause Eisenmenger syndrome.[2] After an asymptomatic period, the syndrome presents in young adults with exertional dyspnea and cyanosis.[3] Prognosis is poor, with 10-year mortality of 30–40% in a recent meta-analysis.[4] Standard therapies for pulmonary arterial hypertension offer limited benefit in this condition and defect closure is traditionally contraindicated because of very high mortality.[5] The only 'curative' intervention is heart–lung transplantation, with its attendant risks of death, infection and rejection. Given its complexity and the scarcity of donor organs, transplantation in Eisenmenger syndrome is a last resort.

In a 1977 *Lancet* article, Batista claimed successfully reversing pulmonary arterial hypertension in a 19-year-old woman with a congenital ventricular septal defect and atrial septal defect by pulmonary artery banding.[6] Afterwards, the right-to-left shunt increased sharply, perilously decreasing aortic oxygen saturation to 60–75% and pulmonary artery oxygen saturation to 20%. Pulmonary vascular changes reportedly regressed and, a year later, the pulmonary artery was de-banded and the septal defects closed. Batista proposed that lower pulmonary artery saturation dilated the pulmonary vascular bed, asserting that

> *People believe that pulmonary hypertension in the Eisenmenger complex is due to hyperflow. We say that hypertension is not caused by hyperflow, at least not primarily. We postulate that high pulmonary-artery oxygen saturation is the main cause of pulmonary-artery vasoconstriction and pulmonary-artery vascular resistance.*

If pulmonary vasculature truly vasoconstricts in response to high pulmonary artery oxygen, lower pulmonary artery oxygen concentration would result in pulmonary vascular dilatation and regression of Eisenmenger pathology. It is difficult to draw firm conclusions from this case with neither peer review nor follow-up since 1997, although Batista has presented other similar cases at conferences. Nevertheless, circumstantial evidence supports a relationship between high pulmonary artery oxygen saturation and vasoconstriction. Isolated pig lungs showed marked pulmonary vasodilatation when pulmonary artery oxygen saturation was reduced.[7] When crocodiles and other aquatic reptiles dive, a right-to-left shunt diverts most of the pulmonary blood flow towards the systemic circulation.[8] This makes biological sense as there is little point in pumping blood to unventilated lungs. A similar mechanism operates in the ductus arteriosus of unborn humans. Alveolar hypoxia is known to cause pulmonary vasoconstriction, indicating that there are oxygen sensors within the lungs. It is possible that such sensors respond not to alveolar oxygen saturation, but to the oxygen gradient across the alveoli. If so, pulmonary vasoconstriction could be as much a consequence of pulmonary artery oxygen rise as of alveolar oxygen fall. Furthermore, if pulmonary vasoconstriction in Eisenmenger syndrome occurred purely because of high flow, it should plateau as pulmonary arterial hypertension develops and systemic and pulmonary flows equalise. Pulmonary artery oxygen saturations, however, do not return to normal, as most Eisenmenger patients have bidirectional shunting across the defect[9] (due to beat-to-beat variation in atrial return and downstream compliance). Bidirectional shunting maintains abnormally high pulmonary artery oxygen content.

Batista's method of tight pulmonary artery banding raises right-sided pressures to supra-systemic levels, abolishing left-to-right shunting, but with inherent risks: hypoxic patients become even more hypoxic and the right ventricle faces a sudden, further increase in afterload. We propose an alternative: to close the defect using a valve rather than a patch, preventing left-to-right shunting while allowing right-to-left flow, so that the right heart can offload in pulmonary arterial hypertension crises. If Batista is correct about the impact of pulmonary artery oxygen saturation, this would prevent highly oxygenated blood from reaching the pulmonary artery to cause constriction. Over time, pulmonary arterial hypertension decreases, right-sided pressures fall and the valve would remain closed, obviating the need for a second operation.

Previous attempts at closure of intracardiac defects using patch valves and fenestrated patches had variable results[10,11] and it is unclear whether Eisenmenger syndrome was truly established in the patients. Our proposal is attractive as a simple approach to prevent potentially fatal right ventricular failure after defect closure in Eisenmenger patients. It may be achievable percutaneously with transcatheter valve technology and surgically with existing bioprostheses and current myocardial protection. We believe that this should be explored further as a treatment as it is unlikely to cause harm and may have substantial benefit.

Eisenmenger syndrome has few treatment options. The hypothesis of high pulmonary artery oxygen saturation as a cause for the pulmonary vascular changes encourages the exploration of valved closure of intracardiac defects associated with a bidirectional shunt in the hope of reversing the vascular changes without compromising the right ventricle.

Declarations

Competing Interests: None declared.

Funding: None declared.

Ethics approval: Not required.

Guarantor: SAMN.

Contributorship: LM performed the literature search and co-wrote the manuscript. LF provided expert knowledge, additional literature search and reviewed the manuscript. SAMN conceived the idea and co-wrote the manuscript.

Acknowledgements: None.

Provenance: Not commissioned; peer-reviewed by Tom Treasure.

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