

to the higher metabolic needs and improve the systemic perfusion an echocardiography-guided optimization of BiVAD pump parameters was performed. Results: In BiVAD-supported patients, the increased metabolic and circulatory demands associated with sepsis cannot be adequately met due to limited or absent native cardiac reserve. Compensatory mechanisms as tachycardia and enhanced myocardial contractility are absent or markedly blunted. Moreover, the absence of pulsatile blood flow leads to impaired regulation of vascular tone. This results in a dissociation between pump flow, arterial pressure, and tissue perfusion. Sepsis-induced systemic vasodilation further aggravates the imbalance between fixed or semi-fixed cardiac output and reduced systemic vascular resistance, creating a complex hemodynamic state characterized by features of both cardiogenic and distributive shock. Even though an integrated therapeutic approach incorporating pump flow optimization and multimodal organ support in this case was associated with favorable clinical outcome, the treatment is significantly prolonged. Conclusion: The coexistence of constrained cardiac output and sepsis-induced vasodilation in a patient supported with BiVAD produces a mixed form of cardiogenic and distributive shock with impaired compensatory mechanisms. Recognition of this unique hemodynamic profile is essential for appropriate monitoring and therapeutic strategies. To achieve a hyperdynamic response, a multimodal management strategy is required, in which pump flow may be adjusted, with careful consideration of the associated risk of suction events.

Haemodynamic-energetic mechanism of sudden cardiac death in severe aortic stenosis: A modelling study

Martin Dvouletý¹, Michal Šitina^{1, 2, 3, 4}

¹Department of Pathological Physiology, Faculty of Medicine, Masaryk University, Brno, Czech Republic

²Department of Internal Medicine I, Cardiology and Intensive Care Medicine, Landesklinikum Mistelbach-Gänserndorf, Mistelbach, Austria

³Biostatistics, International Clinical Research Center, St. Anne's University Hospital Brno, Czech Republic

⁴2nd Department of Internal Medicine, St. Anne's University Hospital in Brno, Czech Republic

Introduction: Severe aortic stenosis (AS) is a recognized risk factor for sudden cardiac death (SCD). While ventricular tachyarrhythmias are the most common immediate cause of SCD, the majority of cases of SCD in patients with severe AS exhibited bradyarrhythmia as the primary rhythm. Enhanced activation of left ventricular baroreceptors (Bezold-Jarisch reflex) has been implicated in the pathogenesis of syncope in patients with AS. However, the precise mechanism by which an otherwise benign circulatory syncope can progress to cardiac arrest in severe AS remains unclear. We propose a hemodynamic-energetic mechanism to explain this progression and demonstrate its plausibility using a mathematical model of cardiac hemodynamics and energetics. **Methods:** The mathematical model of cardiac hemodynamics and energetics developed in this work is based on the two-element Windkessel model of arterial hemodynamics, the

ventriculoarterial coupling model, and ventricular energetics model. The model quantifies energy delivered to the heart by the coronary circulation and energy expenditure of the heart. Under physiological conditions, energy delivery is higher than energy expenditure. Using the model, we examined whether and under which circumstances the opposite situation can arise where energy expenditure is higher than energy delivery. Such a situation does not allow more than very short-term cardiac function and leads inevitably to cardiac arrest. To analyze the model, the influence of individual independent model variables on energies, pressures and stroke volume was assessed, and global sensitivity analysis was performed using Sobol indices. Simulations of syncopal episodes were performed for individuals with a normal aortic valve and with severe AS. Four scenarios were assessed: resting state, isolated pronounced reduction in total peripheral resistance (TPR), TPR reduction with compensatory response, and TPR reduction with concomitant bradycardia. The model was validated against published clinical data to ensure physiological plausibility and consistency. **Results:** The model identifies states of cardiac energetic imbalance, wherein the energy expenditure of the heart exceeds the energy delivered to it. Analysis of individual independent variable influence indicates that an energy imbalance in AS is precipitated by low aortic valve area (Sao), low TPR, high left ventricular end-diastolic volume (EDV), high end-systolic elastance, high heart rate (HR), low arterial compliance and high coronary vascular resistance (Rcor). Global sensitivity analysis shows that in normal aortic valve or non-severe AS, energy balance is primarily determined by Rcor, TPR and HR, with Rcor being dominant. In severe AS with preserved coronary vasodilatory reserve, Rcor remains most influential, while TPR, Sao and EDV also contribute significantly. When coronary vasodilation is impaired in severe AS, Rcor loses relevance, and energy balance depends mainly on Sao, EDV, and TPR. Other variables have minimal impact. The results of simulation of syncopal episode reveal that in an individual with a normal aortic valve, an isolated profound reduction in TPR results in energy destabilization. However, the compensatory response as well as the concomitant bradycardia serve to reverse this imbalance. In contrast, only the resting situation is energetically stable in case of AS. As in the normal case, an isolated profound reduction in TPR results in energy destabilization. However, neither compensatory response nor concomitant bradycardia can reverse the imbalance. **Conclusions:** This study proposes a hemodynamic-energetic mechanism to explain how otherwise benign circulatory syncope can progress to cardiac arrest in patients with severe AS and demonstrates the plausibility of this concept. In individuals with a normal aortic valve, compensatory mechanisms can restore energetic balance during syncope. In contrast, only resting state is energetically stable in severe AS; all conditions involving low TPR are energetically unstable, regardless of compensatory response. As energy imbalance is incompatible with sustained cardiac function, it inevitably leads to death. The proposed mechanism does not require an exaggerated Bezold-Jarisch reflex, although this reflex likely acts as a trigger of syncope.

REFERENCES

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