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Refractory microvascular angina in hypertrophic cardiomyopathy: a novel therapy?

We read with interest the article by Jex *et al.*[1] of a case of refractory angina in the context of hypertrophic cardiomyopathy (HCM) and Type 2 diabetes mellitus. The authors report a long duration of follow-up and discuss the contribution of diabetes mellitus to the pathological process of HCM resulting in accelerated myocardial fibrosis and refractory angina secondary to coronary microvascular dysfunction (CMD) despite trials of at least four anti-anginal medications.

The association between HCM and CMD is well known. Hypertrophic myocardium is often less vascularized resulting in a mismatch between myocardial oxygen supply and demand, and ischaemia is often seen as a circumferential perfusion defect on cardiac magnetic resonance imaging (MRI).[2] Few evidence-based anti-anginal therapies exist for these patients.

Refractory angina represents a significant global clinical burden, most commonly due to advanced epicardial coronary artery disease. This case serves to highlight that refractory angina may be secondary to disorders of the coronary microcirculation either in isolation or combination with established epicardial coronary artery disease.[3] Although effective anti-anginal treatments are limited for these patients, one potential therapy which has an increasing evidence base is Coronary Sinus Reducer (CS Reducer) implantation.

The CS Reducer is an hourglass-shaped stainless-steel device that is inserted percutaneously into the coronary sinus and produces a controlled narrowing of the venous outflow of the heart. Given a Class IIb, level of evidence B recommendation by the European Society of Cardiology Chronic Coronary Syndromes Guidelines, its use is supported by a randomized, double-blinded, sham-controlled clinical trial, and multiple large-scale prospective registries.[4,5] Furthermore, it has recently received NICE guidance in the UK.[6]

The use of the CS Reducer in CMD may be of particular interest given its proposed effects on the coronary microcirculation. Hypothesized to increase venous backpressure, recruit collaterals, and redistribute blood flow from non-ischaemic to ischaemic myocardium, the CS Reducer is a biologically plausible therapy that may benefit patients with CMD. However, this has not been conclusively evaluated to date. Preliminary evidence from a small study using semi-quantitative stress perfusion MRI has suggested improvements in myocardial perfusion reserve index in ischaemic segments and case reports have suggested improvements in invasive physiological indices of CMD such as coronary flow reserve and index of microvascular dysfunction.[7] Several ongoing studies utilizing both functional perfusion imaging and invasive coronary physiology aim to uncover the mechanism of action of CS Reducer (NCT04892537 & NCT05492110). In this case report, stress myocardial blood flow fell a greater extent over time (2.63–0.75 mL/min/g) than the rest myocardial blood flow (0.9–0.6 mL/min/g) suggesting a structural endotype of CMD. Whether coronary sinus reduction may differentially benefit structural as compared with functional endotypes warrants further investigation and will help inform the development of future therapies tailored to an individual's physiological phenotype.

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