Invasive Coronary Microvascular Function Assessment: Pharmacological vs Exercise Testing

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Coronary microvascular dysfunction is characterised by functional and/or structural abnormalities[1]. It is associated with acute and chronic coronary syndromes, heart failure, non-ischaemic cardiomyopathies and impaired prognosis[2–6]. Since the heart is a deep organ, safe and accurate assessment of coronary microvascular function is challenging. Myocardial ischaemia is a blood supply: demand problem (**Figure 1**). Most research into coronary microvascular dysfunction is focused on perturbations in blood supply. Few studies of myocardial metabolism, particularly during exercise, have been undertaken.

The mechanistic study by Noaman et al. [7] provides new insights. Twenty-four patients presenting with myocardial injury, infarction or ischaemia with no obstructive coronary artery disease (MINOCA or INOCA) underwent microcirculatory resistance and myocardial metabolic assessment at the time of invasive coronary angiography. Microvascular resistance was measured in the left anterior descending coronary artery using coronary thermodilution. Measurements were taken at rest (basal resistance) and during hyperaemia (index of microvascular resistance [IMR]) induced by intravenous adenosine infusion. These measurements were then repeated after a graded exercise regime using a table-mounted ergometer. The microvascular findings were paired with transcardiac metabolic biomarkers as measured by blood sampling from the aorta and coronary sinus.

When stratified according to pre-exercise IMR, patients with a high IMR versus a normal IMR demonstrated: persistently lower coronary blood flow, higher microvascular resistance, blunted oxygen extraction, and increased lactate uptake during exercise. Further, the high IMR group had elevated transcardiac gradients of NT-proBNP and troponin following exercise. These differences suggest divergent pathophysiological phenotypes, which may identify different vascular and metabolic targets for therapy.

Pharmacological vs Exercise-Induced Hyperaemia

Pharmacological hyperaemia is a reference method for assessing microvascular function during invasive coronary angiography. Exercise stress testing is an alternative approach, albeit with logistical considerations. Further, exercise and pharmacological stress testing have differential haemodynamic effects. For example, adenosine-mediated hyperaemia decreases diastolic blood pressure secondary to vasodilation, whereas exercise increases systolic and usually diastolic blood pressure.

Noaman et al. proposed peri-procedural physiological stress as a complementary approach to adenosine-mediated hyperaemia. This combined approach has the potential to provide additional information relating to the effects of physical exercise, including myocardial and microcirculatory autoregulation, and metabolic efficiency. This approach to stress testing in the cardiac catheter laboratory more closely mimics the physiological changes during daily activity. Noting the limitations of the modest sample size, most patients in this study experienced a paradoxical increase in microvascular resistance during exercise.

This study had limitations, notably the sample size and selected population. While the authors have highlighted logistical challenges in performing these studies, further research seems justified. Future studies should incorporate controls for exercise and metabolic assessments, even if non-invasive tests (e.g. cardiac MRI) were adopted. The next steps could include studies of the associations between coronary flow reserve (CFR) and metabolic changes during adenosine versus exercise-induced stress. Invasively measured CFR is an important tool for the diagnosis of microvascular angina, given the well-established associations between invasive CFR and non-invasive ischaemia tests, and prognosis.

Application in clinical practice

The study population was heterogeneous. The inclusion of patients with MINOCA but without comprehensive investigation, like intravascular imaging and cardiac MRI, introduces data gaps, including on coronary and myocardial pathology.

The advantage of peri-procedural exercise testing lies in its improved disease stratification. The authors propose a more precision-based approach targeting endothelium or metabolic pathways, depending on the results. This may link with disease modification through aerobic exercise training and increased nitric oxide production [8].

Exercise ergometry in the catheter laboratory introduces non-trivial logistical and time considerations. In this study, the mean exercise duration was 8.5 minutes, excluding equipment setup. These logistical considerations may limit diffusion to wider clinical practice. The patient's ability to exercise is also relevant and performance may vary greatly depending on motivation and co-morbidities. Safety is always a primary consideration. No procedure-related complications were reported, despite coronary instrumentation during exercise, which is commendable.

Nonetheless, controlled exercise stress testing in the catheter laboratory may be helpful in selected patient groups.

Conclusions

Exercise-induced hyperaemia using a table-mounted ergometer during invasive coronary angiography is feasible and enriches the understanding of the patient's microcirculation during physiological stress. This lends insights into future targets for stratified therapy.

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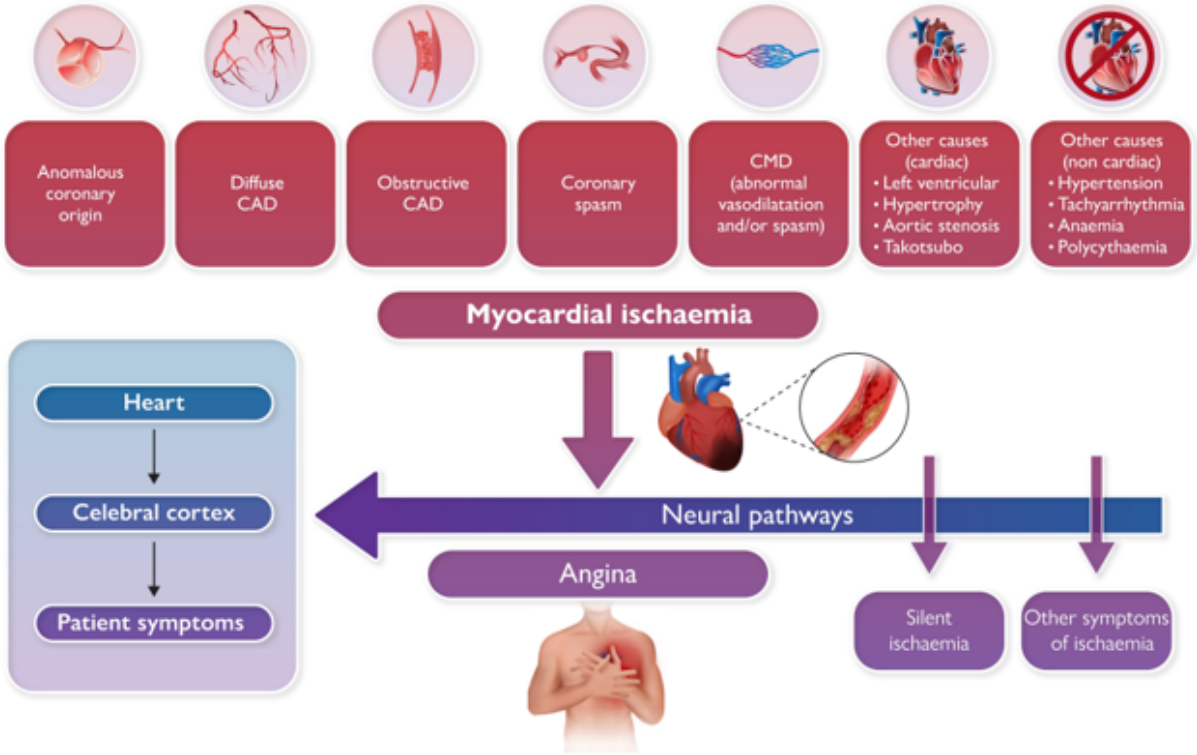
Figure 1. Differential aetiology of myocardial ischaemia.



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