Heartbeat: oxygen transport close to and far from the ventricle in heart failure

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In patients with heart failure with reduced ejection fraction, impaired oxygen delivery to peripheral muscles is blunted due to left ventricular systolic dysfunction with a reduced stroke volume reserve during exercise. Hearon and colleagues¹ hypothesised that patients with heart failure with preserved ejection fraction (HFpEF) also might have impaired oxygen delivery and utilisation (VO_2 kinetics) in response to increased skeletal muscle metabolic demands during exercise. In a series of 19 patients with HFpEF, compared to 18 control subjects, there were markedly slower rates of maximal oxygen utilisation due to impaired peripheral oxygen extraction, despite a normal increase in submaximal cardiac output with exercise (figure 1). The authors suggest that impaired peripheral oxygen utilisation might be a target for therapy in patients with HFpEF.

In the aptly titled editorial 'Package delivered, message not received', Borlaug² concludes that 'there are many steps in the O_2 transport pathway that become compromised in people with HFpEF. Hearon and colleagues¹ have reminded us how the final steps in this pathway are often just as limiting as the more central steps closer to the heart, and in the process, they have elegantly demonstrated how we may be able to use VO_2 kinetics to help identify the patients where these peripheral steps become most compromised (figure 2). If the mail is not being delivered, we need to know why, and the same is true if O_2 transport is constrained. It is hoped that with more robust phenotyping methods, using VO_2 kinetics and other novel methods, we will one day be in a position to better understand the nature of deficits in both the heart and periphery at the individual patient level, enabling better tailoring of therapies to improve clinical status for this large and ever expanding cohort'.

The diagnosis of acute myocardial infarction (AMI) can be challenging in patients with a left bundle branch block (LBBB) on electrocardiography.

Figure 1 (A) Representative breath-by-breath ventilatory oxygen uptake kinetics in a HFpEF patient (blue) and a healthy control subject (black). Breath-by-breath oxygen utilisation (VO_2) was measured during submaximal treadmill exercise, interpolated linearly at 1 s intervals and fitted using on-transient monoexponential curve fitting. (B) Mean response curves for controls HFpEF patients and HFpEF patients stratified by mean response time (MRT) modelled using group average amplitude ($\Delta \text{VO}_2 = \text{steady state } \text{VO}_2 - \text{baseline } \text{VO}_2$) and MRT, defined as the exponential time constant of VO_2 onset kinetics, which reflects the time needed for oxygen uptake to rise to ~63% of steady state VO_2 . HFpEF, heart failure with preserved ejection fraction.

Nestelberger and colleagues³ examined the diagnostic performance of ECG criteria and high-sensitivity cardiac troponin (hs-cTn) compared with a centrally adjudicated diagnosis of AMI using the universal definition of myocardial infarction in a series of almost 9000 patients who presented with chest pain. A LBBB was present in <3% of patients and only 30% of these patients had an AMI, with no difference between those with a new or known LBBB. In patients with LBBB, ECG criteria alone were specific (95%–100%), but not sensitive (1%–12%), for diagnosis of AMI. In contrast, a diagnostic algorithm

Figure 2 Schematic representation of oxygen consumption (VO_2) kinetics. VO_2 (red line) is plotted as a function of time during constant workload exercise. The mean response time (MRT) represents the time required for VO_2 to rise to ~63% of steady-state level at a given exercise workload. In health, VO_2 rises very rapidly during exercise, because both the convective and diffusive components of the O_2 transport pathway are able to respond rapidly and efficiently to increasing metabolic demand, with a pattern that more closely resembles an idealised square wave (upper left bounds). In patients with abnormal VO_2 kinetics, there is a progressive lag in the increase in VO_2 , resulting in prolongation of the MRT and an increase in the gap between the square wave and the observed increase in VO_2 (red shaded area). This gap is termed the oxygen deficit, and may be caused by convective or diffusive abnormalities in O_2 transport.

(figure 3) combining ECG criteria with hs-cTn levels at baseline and the change in levels at 1–2 hours, had a high accuracy (97%) for diagnosis of AMI in patients with LBBB.

In an editorial, Glass *et al*⁴ find these results encouraging but caution that 'these data are limited to patients with suspected AMI due to acute coronary occlusion; at the present time, the algorithm cannot be extrapolated to patients presenting with other possible aetiologies for hs-cTn elevation (eg, troponin elevations due to demand ischaemia, sepsis or renal insufficiency)—this issue is the major limitation of this algorithm. Additionally, in patients with LBBB but without ECG changes diagnostic of AMI, negative hs-cTn determinations should not be construed to preclude the need for further evaluation or treatment of alternative, non-AMI causes of chest pain

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Figure 3 Integrated diagnostic work-up in cohort 1. Flow chart representing the integrated diagnostic work-up for patients presenting with left bundle branch block and suspected AMI in cohort one using hs-cTnT. AMI, acute myocardial infarction; hs-cTn, high-sensitivity cardiac troponin; CPO, chest pain onset; LBBB, left bundle branch block; pts, patients.

Figure 4 Comprehensive assessment of NOCAD during the time of angiography. *Evaluation of atheromatous disease can be carried out using resting or submaximal hyperaemic indices based on local practice. §Patients with visible atheroma should be commenced on secondary preventative therapy regardless of final diagnosis. The white area describes tests available on an ad hoc basis in all catheter laboratories, whereas the grey shaded area describes acetylcholine testing that can currently only be performed on a named-patient basis clinically, or within the context of dedicated research protocols, limiting its widespread ad hoc use. CAD, coronary artery disease; CFR, coronary flow reserve; CMD, coronary microvascular dysfunction; FFR, fractional flow reserve; NOCAD, non-obstructive coronary artery disease.

(eg, unstable angina, pulmonary embolism and so on).

Coronary microvascular dysfunction (CMD) increasingly is recognised as a cause of symptoms and predictor of adverse cardiovascular events in the 40% of patients undergoing coronary angiography who are found to have normal vessels or non-obstructive coronary disease. In a comprehensive review article, Rahman and colleagues⁵ summarise the diagnostic and therapeutic approach to these patients and point out

the knowledge gaps needing further clinical research (figure 4).

Other interesting content in this issue includes a review of the clinical presentation and management of pregnancy in women with cardiomyopathy,⁶ the Education in Heart article on cardiac computed tomographic (CT) imaging (figure 5)⁷ and the Image Challenge⁸ case which uses imaging findings to make the diagnosis in 62-year-old women with non-sustained ventricular tachycardia.

Figure 5 An illustration of the application of CCTA for the detection and evaluation of coronary artery disease. Panel A shows a multiplanar reformatted image of the left anterior descending artery illustrating the use of CCTA for detection of CAD in either symptomatic or high-risk asymptomatic individuals. Panel B shows the use of CCTA to evaluate plaque characteristics (ie, degree of calcification) and presence of high-risk findings (in this instance, positive remodelling). Panel C shows the use of CCTA for quantitative plaque assessment while panel D shows the use of CTP for the assessment of coronary physiology in the setting of coronary artery disease. CCTA, coronary CT angiography; CTP, CT perfusion.

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REFERENCES

- 1 Hearon CM, Sarma S, Dias KA, *et al*. Impaired oxygen uptake kinetics in heart failure with preserved ejection fraction. *Heart* 2019;105:1552–8.
- 2 Borlaug BA. Package delivered, but message not received. *Heart* 2019;105:1528–9.
- 3 Nestelberger T, Cullen L, Lindahl B, *et al*. Diagnosis of acute myocardial infarction in the presence of left bundle branch block. *Heart* 2019;105:1559–67.
- 4 Glass G, O'Connor R, Brady WJ. Useful addition to acute myocardial infarction diagnosis in patients with left bundle branch block: an algorithm using electrocardiographic and biomarker analysis. *Heart* 2019;105:1530–2.
- 5 Rahman H, Corcoran D, Aetesam-ur-Rahman M, *et al*. Diagnosis of patients with angina and non-obstructive coronary disease in the catheter laboratory. *Heart* 2019;105:1536–42.
- 6 Schaufelberger M. Cardiomyopathy and pregnancy. *Heart* 2019;105:1543–51.
- 7 Al'Aref SJ, Min JK. Cardiac CT: current practice and emerging applications. *Heart* 2019;105:1597–605.
- 8 Agoston-Coldea L, Agoston R, Horvat D. Ventricular polymorphic arrhythmia in a 62-year-old woman. *Heart* 2019;105:1582–82.