Heartbeat: Age-related changes in the cardiac response to exercise

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Age-related decline in physical performance is inevitable. The heart is not an exception. Nathania and colleagues[1] investigated the relationship between cardiac high-energy phosphate metabolism and cardiac performance using ^{31}P cardiac magnetic resonance spectroscopy and cardiopulmonary exercise testing in young (≤50 years, n=20) and old (≥60 years, n=15) healthy women. They found a positive and significant relationship between cardiac high-energy phosphate metabolism and cardiac performance. In addition, metabolism and peak cardiac power declined with age. They also found that phosphocreatine (PCr)-to-ATP ratio showed a significant positive relationship with early-to-late diastolic filling ratio (r=0.46, P=0.02) and peak oxygen consumption (r=0.51, P=0.01) (figure 1). Although the relationships were only modest and cardiac metabolism was mostly related to contractile function, decreased cardiac metabolism may play a role in the progression of heart failure with preserved ejection fraction (HFpEF) which is the most frequent cause of heart failure in the elderly. Further, modulating cardiac metabolism may lead to improvement of cardiac performance. Although this is a study with a small sample size and limited to women, the role of cardiac metabolism in the evolution of heart failure deserves further study.

In the accompanying editorial, Fragasso[2] discusses the parallels between the ageing changes in cardiac metabolism described in the study by Nathania *et al*[1] and the relationship between PCr/ATP ratios and cardiac function in patients with heart failure. He asks the questions: "Could the described age-related cardiac metabolic phenotype be the pathophysiological basis of heart failure with preserved ejection fraction?" "Could we do something to slow down this apparently irremediable age-related process?" Although these questions remain unanswered, Fragasso suggests that we should "monitor cardiac metabolic levels and try to improve them by effectively dealing with pathological conditions that could be deleterious and adopt healthy lifestyles. Physical exercise and blood pressure and heart rate reduction are certainly among the best and affordable approaches to pursue this aim."

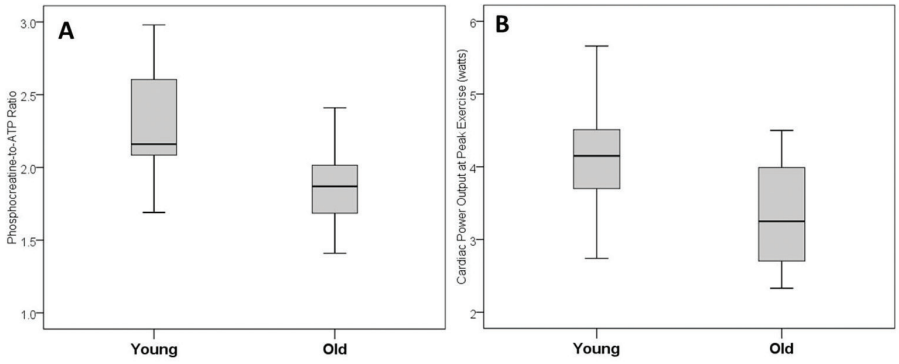

Figure 1 Cardiac high-energy phosphate metabolism phosphocreatine-to-ATP ratio (A) and cardiac pumping capability as a measure of cardiac power output (B)—in young and older women.

Inflammation plays a prominent role in the pathogenesis of atherosclerosis, suggesting the possibility that patients with chronic systemic inflammatory disease might be at increased risk of atherosclerotic cardiovascular disease (CVD). Baena-Díez and colleagues[3] examined this association in a cohort of over 990 000 individuals with no prior history of CVD. In the 0.5% of patients with a systemic connective tissue disorder, such as systemic lupus erythematosus, systemic sclerosis or polyarteritis nodusa, CVD risk was increased with a HR of 1.38 (95% CI 1.21 to 1.57). In the 0.6% with rheumatoid arthritis, the HR for CVD was 1.43 (95% CI 1.26 to 1.62) (figure 2). These data emphasise the importance of appropriate CVD risk stratification and primary prevention in adults with systemic inflammatory diseases. Studies on the role of more aggressive preventative strategies in this patient population are needed.

Microvascular dysfunction occurs in about half of the patients after acute myocardial infarction (AMI) with one-third having irreversible microvascular injury. Early detection of microvascular dysfunction might allow additional interventions to restore myocardial blood flow and prevent long-term adverse outcomes. In a study of 176 AMI patients, de Waard and colleagues[4] found that hyperaemic microvascular resistance (HMR) was superior to invasively measured coronary flow reserve (CFR) for detection of microvascular injury on subsequent cardiac magnetic resonance imaging and for prediction of the composite end point of death or hospitalisation for heart failure (which occurred in 10% of patients) (figure 3).

In an editorial, Maznyczka, McCartney and Berry[5] comment that HMR is a research tool, not ready for routine clinical use due to the technical challenges and time considerations in making this measurement. They argue that "Currently, the index of microvascular resistance (IMR) has the most extensive evidence base to support its use as a reference test of culprit artery microvascular function in patients with acute STEMI. IMR is a thermodilution-derived index, measured using a guide wire that combines a pressure and temperature sensor." However, "Studies in larger cohorts are needed to explore further the utility of IMR and HMR as a therapeutic target during primary PCI and to identify and stratify higher risk patients for more intensive management."

This issue of *Heart* also includes a review of takotsubo cardiomyopathy,[6] summarizing our current understanding of this disease and providing examples of imaging findings (with numerous online videos).

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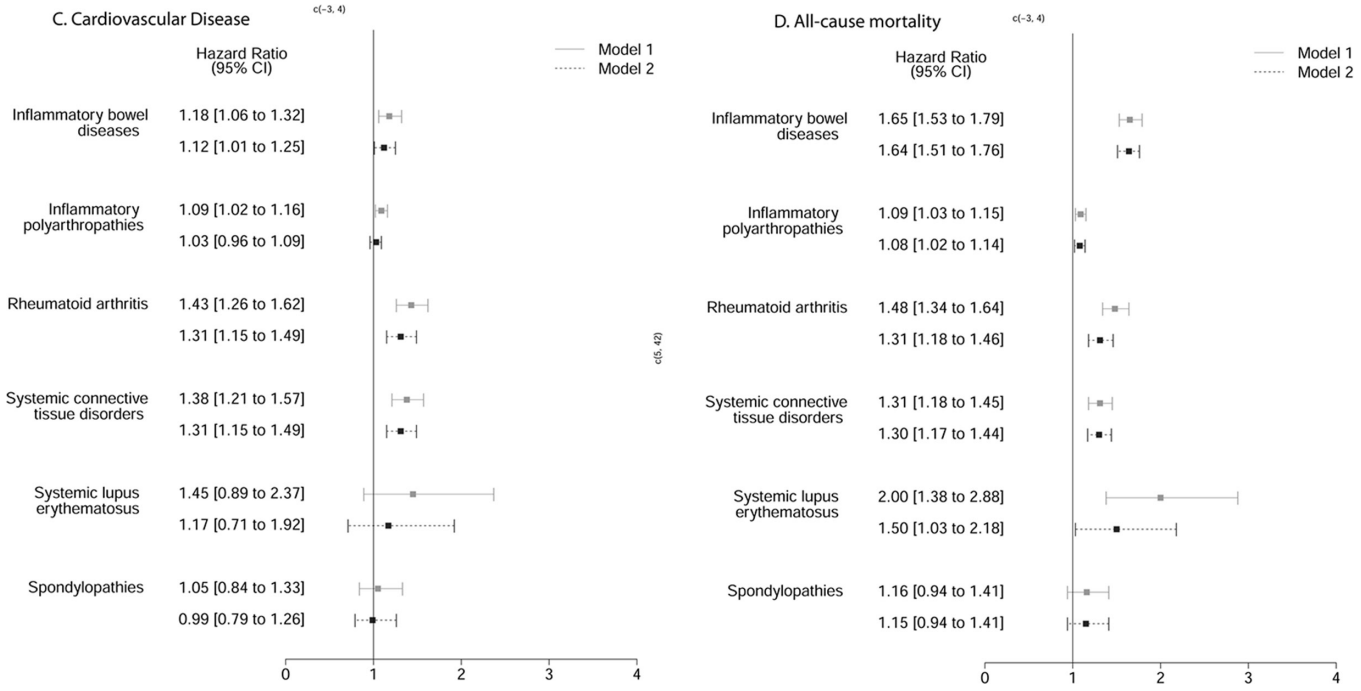

Figure 2 HRs for 6-year incidence of cardiovascular disease (C) and overall mortality (D) among participants with CIID diagnosis compared with those without CIID. Model 1 has been adjusted by age, sex, smoking status, total cholesterol, high-density lipoprotein cholesterol, systolic blood pressure and diastolic blood pressure. Model 2 has been further adjusted for statins, hypertensive drugs and three categories of exposure to antirheumatic-specific treatments: disease-modifying antirheumatic drugs, other anti-inflammatory drugs, no exposure. CIID, chronic immune-mediated inflammatory disease.

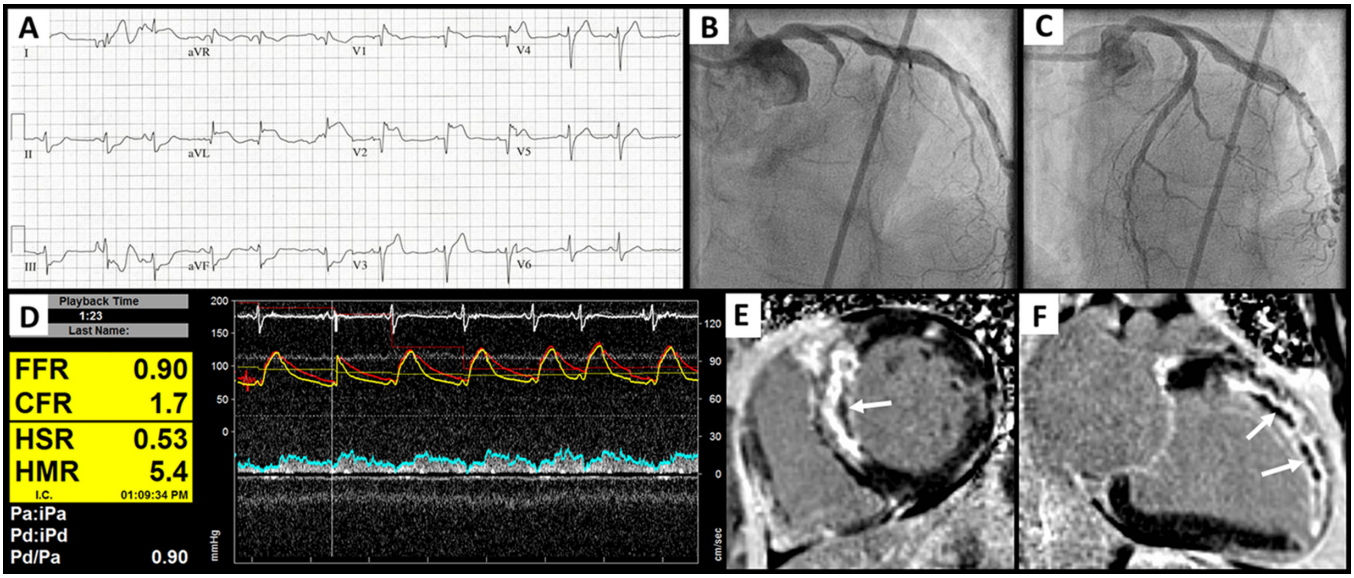

Figure 3 Patient with ST-elevation myocardial infarction enrolled into the study. This patient presented with acute chest pain for 180 min and ST-segment elevation in the anteroseptal leads, with reciprocal depression in the inferior leads (panel A). Emergency coronary angiography was performed showing a proximal left anterior descending artery occlusion (panel B). After primary percutaneous coronary intervention, thrombolysis In myocardial infarction III flow was restored (panel C). Simultaneous Doppler flow velocity and distal pressure measurements were performed in the distal left anterior descending artery (LAD) with intracoronary adenosine 150 µg, yielding a coronary flow reserve (CFR) of 1.7 and hyperaemic microvascular resistance (HMR) of 5.2 mm Hg·cm^{-1} s (panel D). (Panels E and F) Cardiac MRI with late gadolinium enhancement showed a large area of hyperenhancement consistent with an anteroseptal infarction. Within this area, a hypoenhanced core is visible consistent with extensive microvascular injury (indicated by arrows). Panel E is a short-axis view and panel F is a long-axis view. FFR, fractional flow reserve.

The Image Challenge question[7] asks you to make the diagnosis with unusual findings on echocardiography and cardiac magnetic resonance imaging (figure 4), and a concise discussion of the differential diagnosis.

Competing interests None declared.

Provenance and peer review Commissioned; internally peer reviewed.

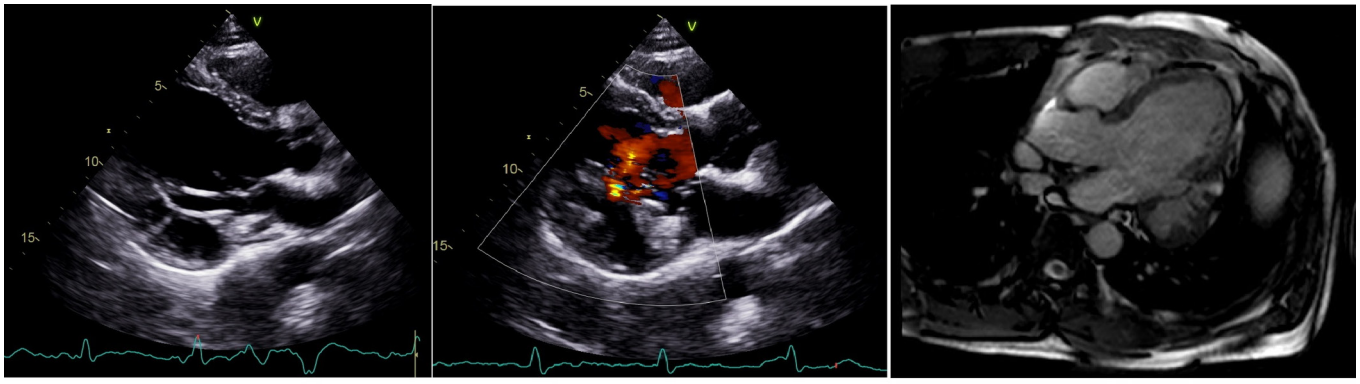

Figure 4 Transthoracic echocardiography (TTE) and cardiac magnetic resonance (CMR). (A) Parasternal left ventricular longitudinal axis view of TTE; (B) colour Doppler of parasternal left ventricular longitudinal axis view of TTE; (C) left ventricular longitudinal axis view of CMR.

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