CARDIAC AND SKELETAL MUSCLE ENERGETIC PATHWAYS FOLLOWING ANTHRACYCLINE CHEMOTHERAPY FOR BREAST CANCER

Background/Introduction Anthracycline-related cardiac dysfunction is a recognised consequence of cancer therapies. Here we assess resting cardiac and skeletal muscle energetic status as an early mechanistic pathway of myocyte derangement and explore molecular targets of skeletal myocyte metabolism, protein synthesis/degradation and mitochondrial biogenesis signalling.

Methods We conducted a prospective, mechanistic, observational, longitudinal study of chemotherapy-naive breast cancer patients undergoing anthracycline-based chemotherapy, compared to a healthy control group. 31P-Magnetic Resonance spectroscopy in cardiac and skeletal muscle (phosphocreatine/phosphomolybdic acid/adenosine triphosphate (PCr/ATP) and inorganic phosphate/phosphocreatine (Pi/PCr) ratios respectively), cardiac magnetic resonance (CMR) imaging inclusive of T1 and T2 mapping, echocardiography-derived global longitudinal strain (systolic -22.9 ± 3.9 % vs -19.1 ± 3.3 %, p<0.001) and CMR-derived ejection fraction (65 ± 5 vs 62 ± 4 %, p=0.001) were assessed before and after 3 cycles of Docetaxel, Epirubicin and Cyclophosphamide followed by 3 cycles of Docetaxel. Statistical significance was set as p<0.05.

Results Twenty-five female breast cancer patients (median age 53 years, range 32 – 74 years) receiving a mean epirubicin dose 307 mg/m2 and twenty-eight controls (median age 44 – 53 years, range 32 – 65) were recruited. All study assessments in breast cancer patients at pre-chemotherapy stage were comparable to the matched healthy controls. However, following chemotherapy, breast cancer patients demonstrated a small but significant reduction in cardiac function (global longitudinal strain -22.9 ± 3.9 vs -19.1 ± 3.3 %, p=0.01) and CMR-derived ejection fraction 65 ± 5 vs 62 ± 4 %, p=0.047), a mild increase in CMR-derived indexed left ventricular volumes (end diastolic 65 ± 10 vs 74 ± 11 ml/m2, p=0.014 and end systolic 23 ± 5 vs 28 ± 5 ml/m2, p=0.01) as well as an increase in left ventricular T1 and T2-mapping (1289 ± 29 vs 1321 ± 31 ms, p=0.004 and 50 ± 4 vs 55 ± 7 ms, p=0.027, respectively) and serum NT-Pro-BNP (49 ± 25 vs 108 ± 84 pg/m, p=0.008). After epirubicin, there was significant reduction in cardiac PCr/ATP ratio (2.0 ± 0.7 vs 1.2 ± 0.6, p=0.007) and a significant increase in skeletal muscle Pi/PCr ratio (0.13 ± 0.04 vs 0.22 ± 0.2, p=0.008) – Figure 1. Following chemotherapy, there was significant upregulation of skeletal myocyte protein synthesis (mammalian target of rapamycin, 0.44 ± 0.4 vs 0.53 ± 0.2, p<0.001) and degradation (Calcium/calmodulin dependent protein kinase II, 1.4 ± 0.7 vs 2.7 ± 1.1, p<0.001), metabolism (peroxisome proliferator-activated receptor gamma, 0.35 ± 0.2 vs 0.60 ± 0.1, p<0.001) and muscle mass regulator myostatin-2 (0.16 ± 0.1 vs 0.24 ± 0.1, p<0.001). Conclusion Contemporary doses of epirubicin for breast cancer result in significant reduction of cardiac and skeletal muscle high energy 31P-metabolism alongside skeletal myocyte alterations of protein synthesis and metabolic regulation pathways.

Conflict of Interest None

MEASURING PCR/ATP AS A MARKER OF MYOCARDIAL ENERGETICS ACROSS THE SPECTRUM OF METABOLIC CARDIAC DISEASE

Introduction Derangements in myocardial energetics are thought to play an important role in the pathophysiology of several cardiac diseases. Myocardial energetics can non-invasively be assessed by measuring the phosphocreatine-to-adenosine triphosphate ratio (PCr/ATP) using 31Phosphorus
magnetic resonance spectroscopy (31P-MRS). Here we compare cardiac PCr/ATP across a spectrum of metabolic cardiac pathologies.

Methods Using a 3D chemical shift imaging sequence and surface coil we recorded PCr/ATP in 433 participants: athletes (n=17), healthy controls with normal weight (n=148), overweight (n=67) and with obesity (n=73), diabetes (n=23), heart failure with preserved ejection fraction (HFpEF) (n=33), heart failure with reduced ejection fraction (HFrEF) (n=63) and amyloid (n=9).

Results A spectrum of myocardial PCr/ATP exists ranging from normal in athletes (2.23 ± 0.28) and those with normal weight (2.05 ± 0.38) to severely impaired in those with cardiac amyloid (1.34 ± 0.19, Figure 1). Despite normal systolic function (all LVEF >57%) those living with obesity and diabetes have lower PCr/ATP than normal (all p<0.001). In all groups with HF, regardless of aetiology, myocardial energetics were impaired (all p<0.001). Across the whole cohort PCr/ATP was negatively correlated with body mass index (r -0.28, p <0.001), age (r -0.34, p<0.001) and LV mass (r -0.1, p<0.001). PCr/ATP was not related to systolic or diastolic blood pressure in these cohorts.

Conclusions Despite normal systolic function, overweight, obesity and diabetes are associated with lower PCr/ATP ratios than normal weight controls. These changes in myocardial energetics appear to exist on a spectrum with further derangement present in overt cardiac pathology. Derangements in myocardial energetics are present in myocardial pathologies independent of underlying aetiology and thus may represent a viable therapeutic target in several conditions.

Conflict of Interest None

Abstract 143 Figure 1

Abstract 144 Figure 1

Introduction Palpitations are a common cause of referral to cardiology clinics for specialist assessment. Although some patients experience true arrhythmias, many have benign ectopic beats only. Echocardiography is routinely performed in such patients, but whether it is required in all patients with palpitations is unknown.

Purpose To analyse the echocardiographic findings in patients presenting with palpitations and assessing the relation of normal echocardiogram with normal physical examination & normal resting 12 lead ECG.

Methods In this single-centre retrospective study, we first obtained a list of all patients seen in the electrophysiology (EP) clinics. Patients with known arrhythmia & known structural heart disease were excluded, as were patients whose presenting complaint was not palpitations (figure 1A). Of the remaining patients, we analysed the notes & clinic letters for physical exam findings and the 12-lead ECG & echocardiogram reports were analysed also. A normal 12-lead ECG was defined by sinus rhythm with normal P-QRS-T waves and intervals. A normal echocardiogram was defined by normal...