relationship between insulin resistance, myocardial energetics and diastolic function, Tyg-I correlated with rest and stress PCr/ATP and rest and stress E/A. In multiple linear regression analysis, the HbA1C was significantly associated with stress MBF (ß= -0.02, p=0.0007).

Conclusion T2D patients show reductions in PCr/ATP, GLS and diastolic function at rest. In response to dobutamine stress, all three groups show similar decrements in myocardial energetics and diastolic function, and similar increments in GLS and LVEF, but with a blunted increment in stress MBF in T2D patients. HBA1c is a predictor of the stress MBF, and rest and stress LVEF show significant associations with rest and stress MBF. Significant associations were detected between the rest and stress energetics and diastolic function, possibly suggesting that diastolic function is a more energetically sensitive process.

Conflict of Interest Nil

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

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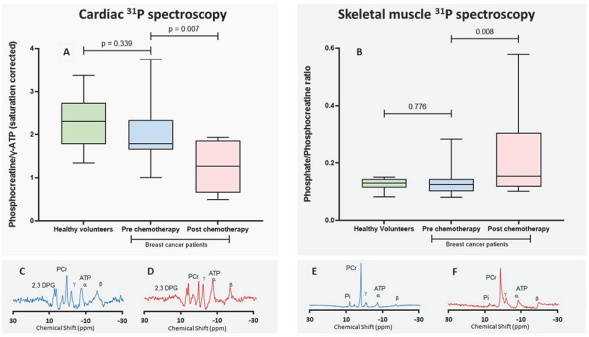
Background/Introduction Anthracycline-related cardiac dysfunction is a recognised consequence of cancer therapies. Here we assess resting cardiac and skeletal muscle energic status as an early mechanistic pathway of myocyte derangement and explore molecular targets of skeletal myocyte metabolism, protein 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/gamma adenosine triphosphate (PCr/γATP) and inorganic phosphate/phosphocreatine (Pi/PCr) ratios respectively), cardiac magnetic resonance (CMR) imaging inclusive of T1 and T2 mapping, echocardiography-derived global longitudinal strain function, serum NT-pro-BNP and skeletal muscle biopsies from the right vastus lateralis were assessed before and after 3 cycles of Flurouracil, Epirubicin and Cyclophosphamide followed by 3 cycles of Docetaxel. Statistical significance was set at 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 years, range 23 - 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/γATP 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).



Abstract 142 Figure 1 31P-MRS cardiac and skeletal muscle energetics. Data shown as median, 25th, and 75th percentile and maximum and minimum (whiskers). A - corrected PCr/ATP and B - Pi/PCr for controls and patients before chemotherapy and after chemotherapy. Example spectra showing: phosphocreatine (PCr), , , and adenosine triphosphate (ATP), and 2,3-diphosphoglycerate (2,3 DPG) peaks before (C) and after (D) chemotherapy; (Pi), phosphocreatine (PCr) and , , and adenosine triphosphate (ATP) peaks before (E) and after (F) chemotherapy

Conclusion Contemporary doses of epirubicin for breast cancer result in significant reduction of cardiac and skeletal muscle high energy 31P-metabolism alongside skeletal myocellular alterations of protein synthesis and metabolic regulation pathways.

Conflict of Interest None

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

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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