reductions in fibrocalcific volume with a novel drug therapy ($\alpha=0.05$, power=80%)

Conclusion Indexed fibrocalcific volume can provide a rapid and robust assessment of fibrocalcific thickening in patients with AS. Fibrocalcific volume correlates well with disease severity, predicts progression and holds promise in tracking disease progression and therapeutic response.

Conflict of Interest None

THE REST AND STRESS RELATIONSHIPS BETWEEN MYOCARDIAL FUNCTION, BLOOD FLOW AND ENERGETICS IN TYPE 2 DIABETES

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Background Coronary microvascular dysfunction (CMD) and compromised cardiac energy production have been proposed as pivotal features underpinning diabetic cardiomyopathy. However, the relative contribution of these two factors to the subclinical functional alterations in type 2 diabetes (T2D) has not been reported.

Objectives Using cardiovascular magnetic resonance (CMR) and 31P phosphorus MR spectroscopy (31P-MRS) we assessed changes in cardiac energetics, perfusion, global longitudinal strain, and systolic and diastolic function in response to dobutamine stress in T2D patients, non-athletic healthy volunteers (HV) and veteran athletes (VA).

Methods Thirty-six T2D patients, 12 VA and 20 HV were recruited. For the stress protocol, intravenous Dobutamine infusion was started at a dose of 10 μg/kg/min and titrated to a maximum dose of 40 μg/kg/min to achieve a target heart rate of 65% of the age-predicted maximum, with ECG and blood pressure (BP) monitoring. Mean rate pressure product was recorded at rest and stress. Target heart rate was maintained for the 31P-MRS and dobutamine stress CMR cine, mitral in-flow and perfusion acquisitions. Triglyceride Index (Tyg-I) was calculated as a measure of insulin resistance.

Results Demographic, biochemical and MRI data are shown in Table 1. Study groups had similar age and sex distribution with no known cardiovascular disease. Resting energetics was significantly lower in the T2D group compared to the VA and HV. Resting PCR/ATP was significantly lower in T2D patients compared to both control groups. Increases in RPP with dobutamine stress were similar across study groups. Significant reductions in myocardial PCR/ATP in response to acute stress were detected in HV and VA with similar percentage change from rest to stress as seen in T2D patients. The rest and stress left ventricular ejection fractions (LVEF) were similar across study groups. However, GLS and mitral in-flow E/A ratios were decreased in T2D at rest. During dobutamine stress, all groups showed similar increases in GLS and similar decreases in mitral in-flow E/A ratio, but these parameters remained higher in the controls. The stress MBF was significantly lower, and the NTproBNP and Tyg-I were higher in the T2D group. The correlations between the cardiac parameters are shown in Fig 1. Rest and stress LVEF correlated significantly with rest and stress MBF. There was no significant correlation between perfusion parameters and diastolic function. Contrary to this, while stress and rest energetics correlated with rest and stress E/A ratios, there was no significant correlation between energetics and LVEF. Suggesting a close

Abstract 141 The Rest and Stress Relationships Between Myocardial Function, Blood Flow and Energetics in Type 2 Diabetes

Abstract 141 Table 1 Demographics, biochemical and CMR characteristics

<table>
<thead>
<tr>
<th></th>
<th>HV</th>
<th>Veteran athletes</th>
<th>T2D</th>
<th>ANOVA</th>
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</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>57 (41-62)</td>
<td>58 (50-64)</td>
<td>59 (57-64)</td>
<td>0.6</td>
</tr>
<tr>
<td>BMI (m)</td>
<td>21 (18-24)</td>
<td>20 (18-23)</td>
<td>23 (21-26)</td>
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<tr>
<td>Body mass index (kg/m²)</td>
<td>25 (23-26)</td>
<td>24 (23-26)</td>
<td>25 (20-28)</td>
<td>0.006</td>
</tr>
<tr>
<td>Fasting glucose (mmol/L)</td>
<td>6.3 ± 4.8</td>
<td>4 (4-5.1)</td>
<td>9.1 ± 6.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cholesterol level (mmol/L)</td>
<td>5.6 (5-6)</td>
<td>5 (5-5.7)</td>
<td>6 (5-8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Triglyceride index</td>
<td>0.7 (0.6-1.2)</td>
<td>0.6 (0.5-1.2)</td>
<td>0.8 (0.6-1.2)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Abstract 141 Figure 1 Correlations between left ventricular ejection fraction (LVEF) at rest and myocardial blood flow (MBF) at rest; LVEF at stress and MBF at stress; Phosphocreatinine/adenosine triphosphate (PCR/ATP) at stress and E/A at stress; PCR/ATP at rest and E/A at rest; PCR/ATP at rest and triglyceride index and E/A at rest and triglyceride index

Values are mean (95% confidence interval).
relationship between insulin resistance, myocardial energetic 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 (β = -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

### Abstract 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 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/phosphocreatine (Pi/PCr) ratios respectively), cardiac magnetic resonance (CMR) imaging inclusive of T1 and T2 mapping, echocardiography-derived global longitudinal strain (GLS) and diastolic function, serum NT-pro-BNP and skeletal muscle biopsies were assessed before chemotherapy and after chemotherapy. Example spectra showing: phosphocreatine (PCr), adenine triphosphate (ATP), and 2,3-diphosphoglycerate (2,3 DPG) peaks before (C) and after (D) chemotherapy; (Pi), phosphocreatine (PCr) and adenine triphosphate (ATP) peaks before (E) and after (F) chemotherapy

**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/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 myocellular alterations of protein synthesis and metabolic regulation pathways.

Conflict of Interest None

### Abstract 143

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

John Aaron Henry, Eylem Levelt, Jenny Rayner, Moritz Hundertmark, Mark Peterzan, Peregrine Green, William Watson, Andrew Lewis, Matthew Burrage, Per Anvidsson, Rebecca Chamley, Ed Nicol, David Holdsworth, Stefan Neubauer, Iadislav Valkovic, Oliver Rider, University of Oxford, Oxford Centre for Magnetic Resonance, University of Oxford, Oxford, Oxford, Iraq OX1 9DU, United Kingdom; Leeds Institute of Cardiovascular and Metabolic Medicine; Oxford Centre for Magnetic Resonance Research; University of Oxford; Faculty of School of Biomedical Engineering & Imaging Sciences, Kings College; Department of Physiology, Anatomy and Genetics, University of Oxford; Division of Cardiovascular Medicine, Radcliffe Department of Medicine, University of Oxford, Nafiona

**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

**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/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 myocellular alterations of protein synthesis and metabolic regulation pathways.

Conflict of Interest None

**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), adenine triphosphate (ATP), and 2,3-diphosphoglycerate (2,3 DPG) peaks before (C) and after (D) chemotherapy; (Pi), phosphocreatine (PCr) and adenine triphosphate (ATP) peaks before (E) and after (F) chemotherapy