flux). The normal heart is metabolically flexible and so should maintain energetics and cardiac output regardless of substrate available for use (fatty acids, FA, or glucose). This flexibility may be impaired in type 2 diabetes mellitus (T2DM), contributing to diabetic cardiomyopathy. However, it is unknown to what extent flexibility can be influenced by artificially altering the substrate available for metabolism.

Purpose To compare cardiac function and energetics in diabetic participants randomised to either Intralipid© or a glycaemic clamp, to increase FA and glucose supply respectively.

Methods At 2 separate visits (> 7 days apart), fasted participants with T2DM and normal cardiac systolic function received intravenous infusions of either 20% intralipid© (Intra, 60ml/hr) or insulin/dextrose 20% (Ins/Dex, variable rate), before undergoing multi-parametric cardiac MRI at 3 Tesla with standard imaging for LV volumes and left ventricular ejection fraction (LVEF), and 31P MR spectroscopy for PCR/ATP ratio and CKkf (s-1). ATP delivery rate was calculated as CKkf .[PCR]. [ATP] was assumed to be 5.7µmol (g wet weight)-1, and [PCr] calculated as PCr/ATP x 5.7.

Results Twelve participants (11 male, age 60.3 ± 7.4 years, BMI 27.9 ± 5.3 kg/m2) were recruited. LVEF was increased on Intra vs Ins/Dex (biplane calculation: 69.1 ± 6.4 % vs 63.3 ± 5.7 %, p=0.007; short axis stack calculation 64.3 ± 4.0 % vs 62.2 ± 4.9 %, p=0.065). In addition, peak circumferential strain was increased on Intra (-20.69 ± 2.26 % vs -18.96 ± 1.72 %, p=0.002). Despite this, altering substrate did not influence PCR/ATP (Intra 1.84 ± 0.37; Ins/Dex 1.80 ± 0.29, p = 0.99), CKkf (Intra 0.15 ± 0.07 s-1; Ins/Dex 0.18 ± 0.09 s-1, p= 0.28) or CK flux (Intra 1.60 ± 0.79 µmol (g wet weight)−1 s-1; Ins/Dex 1.85 ± 0.90 µmol (g wet weight)−1 s-1, p=0.32).

Conclusion Participants with T2DM have increased systolic function when using fatty acid as opposed to glucose as their predominant metabolic substrate. However, there is no change in cardiac energetics, implying either improved metabolic efficiency or increased ATP delivery via a CK independent route.

Conflict of Interest Nil

85 VASOPLEGIA CAUSES HIGH CARDIAC ENERGY DEMAND AND INDUCES CARDIAC PHOSPHOCREATINE DEPLETION: MODELLING HOW 'THE ENGINE RUNS OUT OF FUEL'

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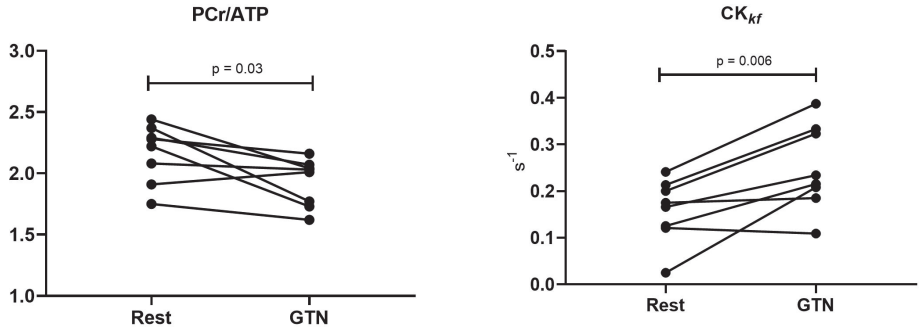
Introduction The healthy heart is at its most efficient when preload is adequate while energy requirements escalate when ionotropy or heart rate are increased. We hypothesized that in vasoplegia, loss of preload (owing to dilation of capacitance veins) and compensatory rises in heart rate and contractility would compromise the efficiency of the heart. We speculated that this may be one factor impairing cardiac function in conditions of distributive shock such as sepsis and looked to model the effects. We used cardiac magnetic resonance imaging to capture changes in cardiac volumes and contractility and magnetic resonance spectroscopy to investigate changes in ATP metabolism within the myocardium.

Methods We recruited 8 healthy volunteers (mean age 41 years, range 28-62 years; mean BMI 22.7, range 18.5-24.5) and measured their baseline cardiac volumes and function, PCr/ATP ratio and Creatine Kinase first order rate constant (CKkf), using cardiac magnetic resonance imaging and magnetic resonance spectroscopy at 3 Tesla. At the same visit, they received a glyceryl trinitrate (GTN) infusion to induce vasoplegia and the measurements were repeated. We targeted GTN infusion rate to a fall in mean arterial pressure of 15mmHg.

Results See table 1. The GTN infusion brought about a fall in mean arterial pressure and a fall in LV end diastolic volume (indicating a reduction in preload) with expected compensatory rises in heart rate and ejection fraction. Cardiac output remained unchanged. Cardiac work (calculated as stroke volume x MAP x heart rate) fell.

Abstract 85 Table 1

Parameter	Baseline	During GTN	p-value (paired t-test)
Mean arterial pressure (mmHg)	78 ± 8	64 ± 7	< 0.0001
Heart rate (bpm)	61 ± 7	69 ± 9	0.0002
Left ventricular end diastolic volume (ml)	166 ± 53	146 ± 56	0.001
Left ventricular ejection fraction	61 ± 3	66 ± 4	0.0008
Cardiac output (L/min)	6.52 ± 1.49	6.56 ± 1.41	0.84
Cardiac work (L.mmHg/min)	459 ± 125	414 ± 114	0.03
PCr/ATP	2.17 ± 0.24	1.93 ± 0.2	0.03
Creatine kinase rate constant (s^{-1})	0.16 ± 0.07	0.25 ± 0.09	0.006
Creatine kinase flux (umol/g/s)	1.76 ± 0.79	2.58 ± 1.07	0.03



Abstract 85 Figure 1

There was a fall in PCr/ATP ratio on GTN, while flux through creatine kinase (indicating rate of generation of ATP from Phosphocreatine) rose and the first order rate constant of the creatine kinase enzyme (CKkf , the rate limiting step in this process) rose by over 50%.

Conclusions The rise in CKkf and CK flux confirm the increased energy demand of the vasoplegic state. What is novel here is that we show a fall in PCr/ATP ratio: as ATP concentrations in the cell are strictly maintained, this suggests phosphocreatine pool depletion occurs when preload is lost and cardiac output is maintained by an increase in inotropy and chronotropy.

Progressive energetic depletion during high demand may give rise to contractile dysfunction over time as the heart is unable to keep up with increased requirements for ATP, which could be a mechanism of cardiac dysfunction during vasoplegia. We hypothesize this could be a contributing factor explaining cardiac dysfunction in sepsis and other conditions of distributive shock.

Conflict of Interest None

86 MITRAL REGURGITATION IN ACUTE HEART FAILURE: PREVALENCE AND RESPONSE TO TREATMENT

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Heart failure (HF) affects an estimated 90 000 people within the UK and 26 million worldwide. As a consequence of ventricular remodelling, significant mitral regurgitation (MR) is common in patients with HF, further contributing to poor prognosis, frequent hospitalisation, and higher rates of mortality. Conventional treatment options for HF patients with MR include medical therapy, cardiac resynchronisation and conventional mitral valve surgery, with transcatheter mitral valve repair reserved for symptomatic patients with left ventricular dysfunction and multiple comorbidities, considered high surgical risk.

Aim Our objectives were to determine: (1) the proportion of patients with an acute HF admission, an EF of <50% and moderate or more mitral regurgitation; (2) the effectiveness of optimal medical therapy in reducing the severity of MR and symptoms for these patients; (3) the number of patients with moderate or more MR, an EF <50% and symptoms despite optimal medical therapy.

Method We performed a retrospective analysis of all patients who presented with acute HF to two large London based tertiary centres over a five year period. Based on a combination of electronic care records, national registry data, and UK Office of National Statistics (ONS) mortality data, we determined baseline symptoms, symptom progression, and comorbidities. Echocardiography data was used to assess the degree of MR and left ventricular systolic function (EF). Where patients underwent subsequent echocardiographic examinations on maximally tolerated medical therapy, the change in the degree of mitral regurgitation, ejection fraction and symptoms (NYHA class) was examined. Logistic regression was used to assess the impact of age, EF and comorbidities.

Abstract 86 Table 1

Baseline Characteristics of patients with Moderate and Severe Mitral Regurgitation

Age (years)	Mean ±SD	78± 20.78
Male	n (%)	76 (56.30%)
eGFR<60	n (%)	70 (63.64%)
NYHA	I	11 (8.15%)
	II	45 (33.33%)
	III	54 (40%)
	IV	25 (18.52%)
Recent MI within 90days	n (%)	11 (9.82%)
Diabetes	n (%)	46 (34.59%)
IHD	n (%)	63 (48.46%)
Hypertension	n (%)	87 (64.93%)

Results Over a five-year period (Jan 2012 – Dec 2017), 1884 patients presented with acute HF. Of this cohort, 302 (16%) had moderate or more MR and an EF of <50%. Mortality amongst patients with moderate or more MR was 29.9% at one year (compared to 26.9% for those with less than moderate MR, p=0.058). Of this cohort, 45% had sufficient clinical and echocardiographic paired follow up data to enable assessment of the effects of optimal medical therapy. This analysis showed, despite optimal medical therapy, all 135 patients still had moderate or more mitral regurgitation. When compared with previous echocardiography data, 11 (8.15%) patients showed a reduction in the severity of MR which meant 92% (124) of patient with MR either saw no improvement or worsening of their MR severity. Of those with severe MR, 23% (7) demonstrated an improvement in the degree of MR following optimal medical therapy. Clinically 70 (51.4%) patients had an improvement in symptoms. There was significant improvement in the NYHA class pre and post optimisation of medical therapy (p<0.001) across all grades of MR. Despite optimal medical therapy, 124 (92%) patients with moderate or more MR, EF <50% remained symptomatic.

Conclusions A large portion of patients who present with acute heart failure have moderate or more MR. Although medical therapy is effective in providing some relief from symptoms, the large majority of patients continue to have moderate or more mitral regurgitation. We propose a portion of these patients are potential candidates for transcatheter mitral valve repair according to current international guidelines, and should be considered for further intervention.

Conflict of Interest Nil

87 DEFINING ENDOTHELIAL CD47 SIGNALLING IN HEART FAILURE

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Introduction Cardiac endothelial cell (EC) dysfunction and death is emerging as a key cause of heart failure, particularly in which ejection fraction is preserved (HFpEF). Of most concern, 50% of new heart failure patients are defined as HFpEF, and this is now the largest unmet cardiovascular complication in the field. ECs express the CD47 receptor which is ascribed an anti-angiogenic signalling role via control of nitric oxide signalling. However, more recent evidence suggests that activation of CD47 by its cognate ligand