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Supplementary information

Cardiac intermediary metabolism in heart failure: substrate use, signalling roles and therapeutic targets

In the format provided by the authors and unedited

Supplementary Table 1 | Myocardial metabolic uptake studies in patients

Reference	Ref Number	Patients	Controls	Mean LVEF %	Age (patients vs controls)	Male Sex (patients vs controls)	Fasting	Method	FA uptake (patients vs controls) (% fractional extraction)	Glucose uptake	KB uptake	Lactate uptake	FAO
Increased FAU													
Taylor M. et al. 2001	[1]	Non-ischaemic CM (n=2) + ischaemic CM (n=10)	None	25% ± 6%	64 ± 14	100%	Yes	PET [^{18}F]Fluoro-6-Thia-Heptadecanoic Acid and [^{18}F]FDG i	193 nmol/min/g; supposedly 3-fold more than controls in other studies	123 nmol/min/g; 2-fold less than controls	–	–	ND
Unchanged FAU													
Funada J. et al. 2009	[2]	Idiopathic DCM (n=8), ischaemic CM (1), T2DM (n=5)	Normal heart function (n=10), history of either supraventricular tachycardia or paroxysmal atrial flutter.	32% ± 16%	53 ± 9 vs 47 ±1 4	78% vs 66%	Yes	Art-CS [2H2]palmitate	NEFA: 32 ± 8% vs 33 ± 8%	2.7 ± 3.5% vs 3.8 ± 2 %, ns	βOHB 41 ± 8% vs 32 ± 22 %, ns	27 ± 16% vs 27 ± 9 %, ns	–
Voros G. et al. 2018	[3]	HFrEF (n=15), AS patients with preserved systolic function (n=15)	Control patients (n=15), normal heart and underwent a radiofrequency catheter ablation procedure for atrial fibrillation or flutter	28 ± 8 or 59 ± 3 in AS vs 59 ± 3	71 ± 6 or 76 ± 8 in AS vs 67 ± 8	60% or 27% in AS vs 53%	Yes	Art-CS LC-MS	Ns differences, approximate FAU range from 10 to 14 % with HFrEF<Control<AS	Glucose 1 to 1.8%, ns	βOHB >30% in HFrEF and AS vs 10% in controls	Lactate 12% to 16%, HFrEf<Control<AS	–
Decreased FAU													
Dávila-Román VG. et al. 2002	[4]	Idiopathic DCM (n=7)	Control volunteers (n=12)	27 ± 8 vs 63 ± 8	39 ± 7 vs 26 ± 5	NA	Yes	PET ^{18}-O, ^{11}C-Acetate, ^{11}C-Gluc, ^{11}C-Palm	134 ± 44 (22%) vs. 213 ± 49 (32%) nmol/min/g	247 ± 63 (5%) vs. 125 ± 64 nmol/min/g (2,5%)	–	–	113 ± 50 vs. 205 ± 49 nmol/min/g

Neglia D. et al. 2007	[5]	DCM (n=10)	Control patients (n=6), history of angina-like chest pain, angiographically normal coronary arteries	32±1 vs 58±1	57±3 vs 67±2	70% vs 50%	Yes	(rt-CS, ^{13}C-lactate and 3H-oleate	~60 vs 230 nmol/min/g P<0.05; but 15±5% vs 18±10% ns	~130 vs 70 nmol/min/g, 4±2% vs 1±1%, P<0.05 for both	–	Tracer measured uptake ns, but release reduced by 50%; and 32±11% vs 18±14% , P <0.05	~0.05 vs 0.15 nmol/min/g (3H-H20), or as % of MVO2: 25% vs 50%
HFpEF													
O'Sullivan JF. et al. 2024	[6]	HFpEF (n=20)	Controls (n=13), healthy volunteers	63 ± 5 vs 63 ± 5	70 ± 9 vs 53 ± 8	35% vs 69%	No	Art-CS LC-MS	Increased lipid uptake in male patients with HFpEF only; by rank: PCs the most, followed by Cer, PIs, Hex1Cer, LPCs, LPEs, PSs and TGs	–	–	–	–

Data are provided as shown in the original articles, most often as mean values ± standard deviation or with confidence intervals, n indicates the number of patients. Whenever possible, units were homogenized for comparison. Art-CS, differential analysis of metabolites in arterial versus coronary sinus samples; βOHB, beta-hydroxybutyrate; Cer, ceramides, CM, cardiomyopathy; DCM, dilated cardiomyopathy; Hex1Cer, hexosylceramide; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; KBs, ketone bodies; LC-MS, liquid chromatography coupled to mass spectrometry; LPC, lysophosphatidylcholine; LVEF, left ventricular ejection fraction; PC, phosphatidylcholine; PIs, phosphatidylinositols; PSs, phosphatidylserines; T2DM, type 2 diabetes mellitus; TG, triglycerides.

References

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