

The effect of different anaesthetics on echocardiographic evaluation of diastolic dysfunction in a heart failure with preserved ejection fraction model.

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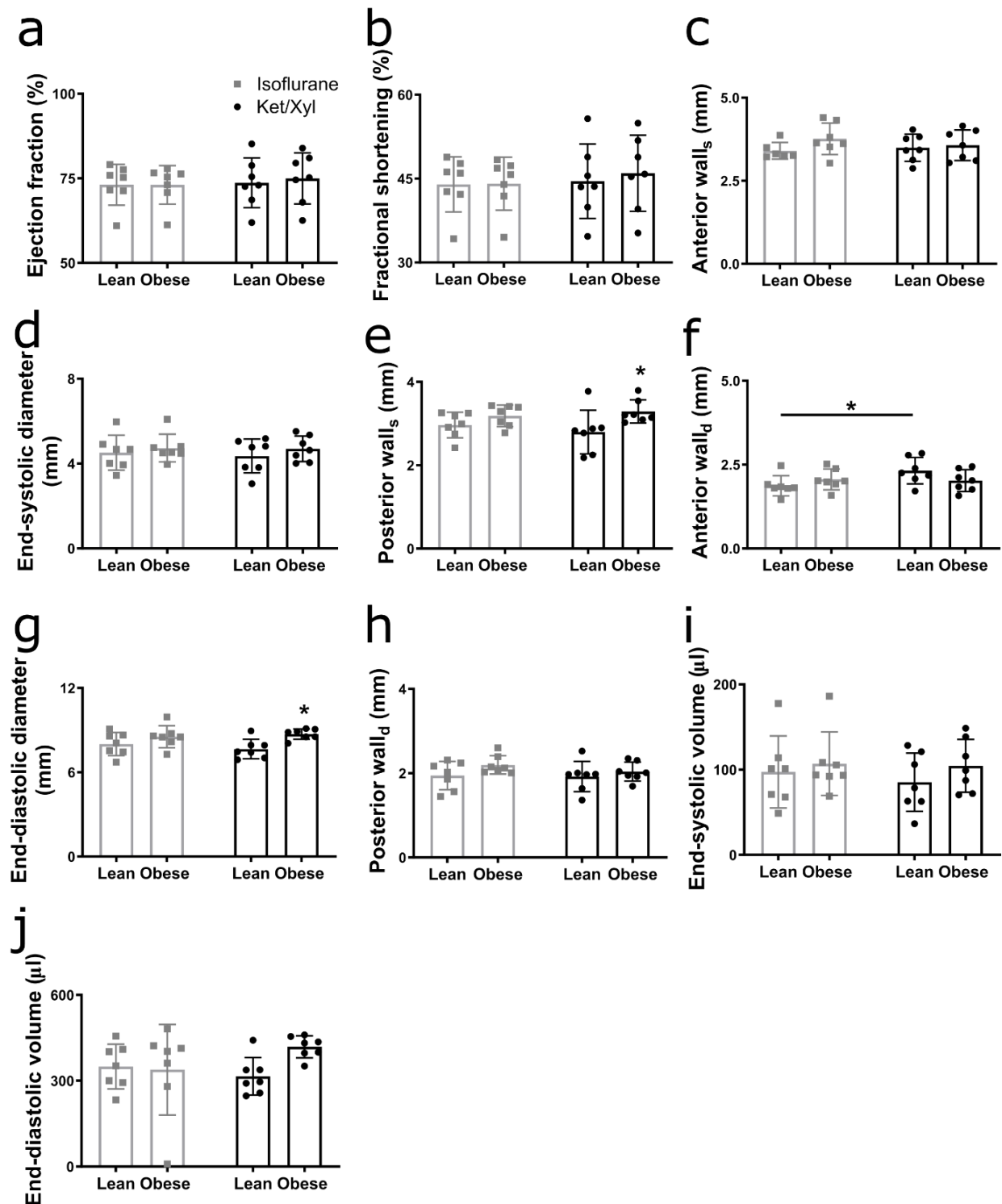
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Supplementary Figures



Supplementary Figure S1- The effects of ketamine/xylazine on systolic function and left ventricular dimension and volumes. Ejection fraction (a), fractional shortening (b), anterior wall thickness in systole (c), end-systolic diameter (d), posterior wall thickness in systole (e), anterior wall thickness in diastole (f), end-diastolic diameter (g), posterior wall thickness in diastole (h), and end-systolic and -diastolic volumes (i,j) in 20-week-old isoflurane- or ketamine/xylazine-anaesthetised lean and obese ZSF1 rats (n=7 per group). Values are presented as mean ± SD. *P<0.05. _d, in diastole; Ket/Xyl, ketamine/xylazine; _s, in systole.

Supplementary Tables

Supplementary Table S1- Echocardiography parameters in isoflurane- or ketamine/xylazine- anaesthetised lean and obese ZSF1 rats

Parameter	Lean- Isoflurane (n=7)	Obese- Isoflurane (n=7)	Lean- Ket/Xyl (n=7)	Obese- Ket/Xyl (n=7)
Heart rate (bpm)	360 ± 20	310 ± 26***	243 ± 25###	200 ± 20**.,###
Stroke volume (µl)	252 ± 43	287 ± 41	230 ± 42	314 ± 46**
Stroke volume, _i (µl/cm ²)	0.51 ± 0.09	0.47 ± 0.07	0.50 ± 0.14	0.52 ± 0.08
Cardiac output (ml/min)	90 ± 12	88 ± 14	55 ± 7.3###	63 ± 12##
Cardiac index (ml/min/cm ²)	0.18 ± 0.02	0.14 ± 0.03*	0.12 ± 0.02###	0.11 ± 0.02##
Anterior wall _d (mm)	1.9 ± 0.3	2.1 ± 0.3	2.3 ± 0.4#	2.0 ± 0.3
Anterior wall _s (mm)	3.4 ± 0.3	3.8 ± 0.5	3.5 ± 0.4	3.6 ± 0.5
End-diastolic diameter (mm)	8.0 ± 0.8	8.5 ± 0.8	7.7 ± 0.7	8.7 ± 0.4*
End-systolic diameter (mm)	4.5 ± 0.8	4.7 ± 0.7	4.4 ± 0.8	4.7 ± 0.6
Posterior wall _d (mm)	1.9 ± 0.3	2.2 ± 0.2	1.9 ± 0.4	2.0 ± 0.3
Posterior wall _s (mm)	3.0 ± 0.3	3.2 ± 0.3	2.8 ± 0.5	3.3 ± 0.3*
End-diastolic volume (µl)	350 ± 78	391 ± 61	316 ± 66	419 ± 39
End-diastolic volume, _i (µl/cm ²)	0.70 ± 0.16	0.64 ± 0.11	0.68 ± 0.20	0.70 ± 0.06
End-systolic volume (µl)	97 ± 42	107 ± 37	85 ± 34	105 ± 31
End-systolic volume, _i (µl/cm ²)	0.20 ± 0.08	0.18 ± 0.06	0.18 ± 0.08	0.10 ± 0.05
Ejection fraction (%)	73 ± 6.0	73 ± 5.7	74 ± 7.4	75 ± 7.5
Fractional shortening (%)	44 ± 4.9	44 ± 4.8	45 ± 6.7	46 ± 6.8
Aortic ejection time (ms)	74 ± 7.5	84 ± 7.4	74 ± 9.9	103 ± 13***.,##
Isovolumic contraction time (ms)	19 ± 3.0	19 ± 2.8	15 ± 3.3	18 ± 2.8
Non-flow time (ms)	125 ± 14	141 ± 11	127 ± 13	167 ± 14***.,##
Myocardial performance index (AU)	0.69 ± 0.05	0.67 ± 0.05	0.68 ± 0.04	0.62 ± 0.04*
Systolic peak wave (mm/s)	45 ± 13	37 ± 4.0	40 ± 3.0	33 ± 9.8
E'/A'	1.7 ± 0.8	1.3 ± 0.4	2.3 ± 0.84	3.0 ± 0.53*.,###

Values are presented as mean ± SD. A', late mitral annulus peak velocity; _d, in diastole; E', early diastolic mitral annulus peak velocity; _i, indexed for body surface area, calculated as 9.1 * body weight in grams^{2/3}; _s, in systole. *P<0.05, **<0.01, and ***<0.001 comparing ketamine/xylazine- or isoflurane-anaesthetised Lean versus Obese rats. #P<0.05, ##<0.01, and ###P<0.001 comparing isoflurane- versus ketamine/xylazine-anaesthetised in each group of rats (either Lean or Obese).

Supplementary table S2- Echocardiography parameters of isoflurane-anaesthetised lean and obese ZSF1 rats treated with or without ivabradine.

Parameter	Lean Saline (n=7)	Obese Saline (n=8)	Lean +Ivabradine (n=7)	Obese +Ivabradine (n=8)
Heart rate (bpm)	369 ± 47	317 ± 28*	302 ± 41 ^{###}	258 ± 19 ^{*,###}
Stroke volume (µl)	291 ± 18	328 ± 31	399 ± 62 [#]	359 ± 31
Stoke volume, _i (µl/cm ²)	0.53 ± 0.04	0.50 ± 0.09	0.61 ± 0.11	0.54 ± 0.10
Cardiac output (ml/min)	108 ± 16	104 ± 12	101 ± 23	93 ± 8.7 [#]
Cardiac index (ml/min/cm ²)	0.19 ± 0.03	0.16 ± 0.03	0.18 ± 0.04	0.14 ± 0.03*
Anterior wall _d (mm)	2.1 ± 0.2	2.1 ± 0.2	2.1 ± 0.3	2.1 ± 0.1
Anterior wall _s (mm)	4.1 ± 0.3	3.9 ± 0.3	4.0 ± 0.3	3.8 ± 0.3
End-diastolic diameter (mm)	8.1 ± 0.1	8.8 ± 0.3**	8.5 ± 0.6	9.1 ± 0.3*
End-systolic diameter (mm)	3.7 ± 0.3	4.4 ± 0.2**	3.9 ± 0.5	4.7 ± 0.4 ^{***}
Posterior wall _d (mm)	2.1 ± 0.4	2.0 ± 0.2	2.0 ± 0.2	2.0 ± 0.2
Posterior wall _s (mm)	3.4 ± 0.4	3.2 ± 0.2	3.5 ± 0.2	3.3 ± 0.2
End-diastolic volume (µl)	352 ± 12	421 ± 32**	398 ± 63	460 ± 36*
End-diastolic volume, _i (µl/cm ²)	0.63 ± 0.03	0.64 ± 0.10	0.72 ± 0.12	0.69 ± 0.11
End-systolic volume (µl)	61 ± 11	93 ± 13**	66 ± 19	101 ± 19 ^{***}
End-systolic volume, _i (µl/cm ²)	0.11 ± 0.02	0.14 ± 0.02*	0.12 ± 0.03	0.15 ± 0.02
Ejection fraction (%)	83 ± 3.3	79 ± 2.3	84 ± 3.6	78 ± 3.5**
Fractional shortening (%)	54 ± 3.7	50 ± 2.3	55 ± 4.3	48 ± 4.0**
Isovolumic contraction time (ms)	17 ± 2.3	16 ± 2.4	17 ± 3.0	17 ± 3.4
Aortic ejection time (ms)	63 ± 6.0	82 ± 2.3 ^{***}	66 ± 4.3	90 ± 3.5 ^{***,###}
Non-flow time (ms)	106 ± 7.8	133 ± 3.7 ^{***}	112 ± 5.2 [#]	143 ± 3.8 ^{***,###}
Myocardial performance index E'/A'	0.70 ± 0.08	0.63 ± 0.05	0.70 ± 0.08	0.61 ± 0.06*
E'/A'	0.60 ± 0.17	0.86 ± 0.40	0.69 ± 0.14	1.2 ± 0.3 ^{**}
Systolic peak wave (mm/s)	42 ± 12	38 ± 5.7	48 ± 15	41 ± 5.1

Values are presented as mean ± SD. A', late mitral annulus peak velocity; _d, in diastole; E', early diastolic mitral annulus peak velocity; _i, indexed for body surface area, calculated as 9.1 * body weight in grams^{2/3}; _s, in systole. *P<0.05, **<0.01, and ***<0.001 comparing either isoflurane-anaesthetised Lean and Obese treated with saline or isoflurane-anaesthetised Lean and Obese rats treated with ivabradine. #P<0.05, ###<0.01, and ###P<0.001 comparing ivabradine- versus non-ivabradine-treated isoflurane-anaesthetised in each group of rats (either Lean or Obese).

Supplementary Table S3- Comparison of Ket/Xyl and isoflurane on echocardiography parameters in rats

Condition Strain	Age(wk) /weight(g)/ Gender (M/F)	Ket (mg/kg)	Xyl (mg/kg)	Isoflurane (%)	Outcome (Ket/Xyl vs Isoflurane)	Reference
Healthy Wistar	Adult/275-325/M	0.1	0.75	1.5	HR ↓ CO ↓ SV = EF = EDD and ESD = PW _d = E ↓ A ↓ E/A =	1
Healthy Sprague Dawley	Adult/330/M	30	5	1.5	HR ↓ CO = SV = EF = EDD and ESD = PW _d ↑ EDV and ESV = S' =	2
Healthy Sprague Dawley	10/ND/M	50	10	1.5	HR ↓ EDD = ESD = (15/30'), ↓ (45') EF = EDV = (15/30'), ↓ (45') ESV = (15/30'), ↓ (45')	3
Healthy Fischer 344	9-12/199-290/M	37	7	1.5	CO ↓ SV = EF = EDD ↓ AW _d = E = A = E/A = DT = IVRT ↑ EDV ↑ AET ↑	4
Healthy Wistar	9/298-306/M	40	8	2.0	HR ↓ CO ↓ EF = EDD ↑ E = A ↓ E/A ↑ DT = E' ↓ E/E' ↓	5
Chronic Aortic Regurgitation Wistar	Adult/275-325/M	0.1	0.75	1.5	HR ↓ CO ↓ SV = EF = EDD and ESD ↓ PW _d = E ↓ A = E/A =	1

A, late mitral inflow peak velocity; AET, aortic ejection time; AW, anterior wall; CO, cardiac output; d, in diastole; DT, deceleration time; E, early mitral inflow peak velocity; E', early diastolic mitral annulus peak velocity; EDD, end-diastolic diameter; EDV, end-diastolic volume; EF, ejection fraction; ESD, end-systolic diameter; ESV, end-systolic volume; F, female; HR, heart rate; IVRT, isovolumic relaxation time; Ket, ketamine; LVID, left ventricular internal diameter; M, male; PW, posterior wall; s, in systole; S', systolic peak wave; SV, stroke volume; Xyl, xylazine. ' indicates the time after the anaesthesia induction.

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