Supplementary Tables.

Table S1. Levels of detection (LOD), levels of quantification (LOQ), and determination coefficients (R^2) of HPLC quantified analytes after the calibration process.

ANALYTES	LOD	LOQ	R2
PYRUVIC ACID	0,000176	0,000535	1
MALIC ACID	0,00156	0,00474	0,9995
LACTIC ACID	0,003	0,008	0,9991
α-KETOGLUTARIC ACID	1,329E-04	0,000402	0,9989
CITRIC ACID	1,009E-03	0,00306	0,9997
FUMARIC ACID	1,478E-05	0,0000447	1
SUCCINIC ACID	0,00287	0,00870	1

Table S2. General characteristics of animals in control (C) and endotoxin (E) groups.

Animal No	C1	C2	C3	E1	E2	E3	E4	E5	E6	E7	E8	E9
Sex	F	F	F	F	F	F	F	F	F	F	F	F
Weight (Kg)	48	50	48	50	52	52	49	48	47	50	50	50
Corporal surface area (m^2)	0.93	0.96	0.93	0.96	0.98	0.98	0.94	0.93	0.92	0.96	0.96	0.96
Age (months)	5	4	4	5	5	5	4.5	5	4	5	4	4
Time to shock (min)				96	129	95	160	270	82	133	360	200
LPS dose (µg)				1429	2052	1469	2435	4128	1126	2039	5000	3145
Median volume of fluid administration previous to T0 (mL).	964	970	1320	1466	1480	1485	1467	1467	1461	1670	1470	1470
Median volume of fluid administration from T0 to T6 (mL).	2472	2560	2472	2560	2648	2648	2516	2472	2428	2560	2560	2560

Table S3. Hemodynamic variables, O_2-derived parameters during the experimental period.

		T0	T3	T6
HR (bpm) *†	**C**	109 (103-111)	106 (86-122)	103 (75-128)
	E	99 (92-103)	141 (97-165)	159 (119-177) ¥
MAP (mmHg) *†	**C**	80 (71-81)	85 (63-92)	75 (73-81)
	E	75 (68-82)	52 (50-59) ‡	55 (44-64) ¥
CVP (mmHg)	**C**	11.6 (7.1-13.3)	12.6 (10.5-13)	10.3 (8-11.3)
	E	11.3 (9.7-13.5)	11.9 (9-12.6)	8.7 (7.4-9.5)
SVR (dyn/cm^5/m^2)	**C**	1297 (1083-1339)	1123 (850-1523)	1016 (1013-1503)
	E	1117 (786-1165)	776 (487-960) ‡	967 (605-1248) §
CO (L/min)	**C**	4.89 (3.24-5.41)	4.34 (4.15-4.99)	5.89 (4.09-6.23)
	E	4.12 (4.05-5.58)	4.3 (4.01-7.66)	5.25 (2.82-7.16)
SV (ml)	**C**	49 (30-51)	47 (36-47)	52 (50-57)
	E	51 (43-55)	40 (33-63)	34 (18-44) ¥
GEDV (ml) †	**C**	556 (474-591)	592 (458-608)	630 (550-636)
	E	504 (467-641)	455 (430-485)	445 (419-452) ¥
DO_2 (mL/min/kg)	**C**	13.82 (6.49-15.18)	11.45 (10.60-12.46)	14.73 (10.03-16.78)
	E	14.48 (11.99-15.46)	14.16 (10.96-17.87)	15.43 (7.79-19.97)
VO_2 (mL/min/kg)	**C**	2.07 (1.86-2.44)	2.35 (1.45-2.37)	2.17 (1.59-3.24)
	E	1.88 (1.83-3.56)	2.23 (1.3-3.29)	2.25 (1.64-2.96)
O_2ER (%)	**C**	19.87 (13.99-28.18)	18.11 (11.96-22.09)	17.14 (11.06-21.34)
	E	16.2 (11.32-23.89)	13.63 (8.94.24.46)	23.20 (11.75-34.99)

Values are represented as medians (interquartile range – IQR). C denotes the control group (n=4); E denotes the endotoxin group (n=9). Differences between groups at each time point were obtained by the Mann–Whitney U test, and differences in the same group at different times were obtained by repeated-measures analysis of variance with Bonferroni correction: * $p<0.05$ at T3 control vs endotoxin, † $p<0.05$ at T6 control vs endotoxin, ‡ $p<0.05$ T0 vs T3 in endotoxin group, ¥ $p<0.05$ T0 vs T6 in the endotoxin group, § $p<0.05$ T3 vs T6 in the endotoxin group. HR: Heart rate; MAP: mean arterial pressure; CVP: central venous pressure; CO: cardiac output; SV: stroke volume; GEDV: global end diastolic volume; PPV: pulse pressure variation; DO_2: oxygen delivery; VO_2: oxygen consumption; O_2ER: oxygen extraction rate

Table S4. Individual data of plasma tricarboxylic acid cycle intermediates obtained by HPLC analysis.

	CITRATE µM/L			KETOGLUTARATE µM/L			SUCCINATE µM/L			FUMARATE µM/L			MALATE µM/L		
Animal Nº	**T0**	**T3**	**T6**	**T0**	**T3**	**T6**	**T0**	**T3**	**T6**	**T0**	**T3**	**T6**	**T0**	**T3**	**T6**
Endotoxin 1	316,67	403,33	500	83,33	103,33	70	76,67	786,67	1296,67	2,1	4,97	4,22	1,36	1,39	5,54
Endotoxin 2	190	290	303,33	30	50	53,33	303,33	1270	90	5,13	4,3	1,7	0,27	0,29	0,41
Endotoxin 3	230	106,67	913,33	40	43,33	110	400	403,33	1063,33	3,04	2,3	65,9	0,25	0,45	0,52
Endotoxin 4	10	110	453.1	40	30	33,33	370	482,5	582,5	5,27	10,47	9,45	0,43	0,03	0,74
Endotoxin 5	156,67	500	540	57,5	62,5	70	513,33	586,67	842,5	3,73	6,17	4,1	0,87	0,55	0,67
Endotoxin 6	313,33	186,67	546,33	40	80	110	7,23	646,67	630	3,67	52,5	12,67	0,4	1,34	3,85
Endotoxin 7	46,67	3686,67	430	220	46,67	63,33	716,67	263,33	700	2,8	4,4	7,43	0,81	0,95	0,82
Endotoxin 8	933,33	320	416	63,33	86,67	120	350	693,33	783,33	42,97	6,89	7,03	1,14	1,62	1,29
Endotoxin 9	170	233,33	333,33	83,33	80	76,67	406,67	693,33	646,67	4,93	4,2	4,43	0,83	1,51	1,07
MEDIAN	*190*	*290*	*453,1*	*57,5*	*62,5*	*70*	*370*	*646,67*	*700*	*3,73*	*4,97*	*7,03*	*0,81*	*0,95*	*0,82*
RIQ1	*156,67*	*186,66*	*416*	*40*	*46,67*	*63,33*	*303,33*	*482,5*	*630*	*2,04*	*4,3*	*4,22*	*0,4*	*0,45*	*0,67*
RIQ3	*313,33*	*403,33*	*540*	*83,33*	*80*	*110*	*406,67*	*693,33*	*842,5*	*5,13*	*6,88*	*9,45*	*0,87*	*1,39*	*1,29*

Control 1	10	40	75	53,33	42,5	70	607	312,5	323,3	2,85	0,79	3,18	1,56	1,16	1,2
Control 2	215	446,67	180	46,67	60	83,33	1210	883,33	160	6,07	7,6	4,93	0,55	0,71	0,56
Control 3	296,67	33,33	286,67	413,33	190	173,33	173,33	156,6	156,67	3,67	4,23	8,33	1,84	1,69	1,79
Control 4	296,67	213,33	200	213,33	236,67	266,67	440	516,67	453,33	4,19	63,53	66,6	0,61	0,63	0,65
MEDIAN	*255,835*	*126,665*	*190*	*133,33*	*125*	*128,33*	*523,5*	*414,585*	*241,65*	*3,93*	*5,915*	*6,63*	*1,085*	*0,935*	*0,925*
RIQ1	163,75	38,33	153,75	51,66	55,62	80	306,67	273,54	159,17	3,46	3,37	4,49	0,6	0,69	0,63
RIQ3	296,67	271,67	221,67	263,33	201,66	196,67	825	608,33	355,81	4,66	21,58	22,9	1,63	1,29	1,35

Table S5. Individual data of plasma lactate, pyruvate and L/P ratio obtained by HPLC analysis.

	PYRUVATE mM/L			LACTATE mM/L			L/P RATIO		
Animal Nº	**T0**	**T3**	**T6**	**T0**	**T3**	**T6**	**T0**	**T3**	**T6**
Endotoxin 1	1,45	1,5	1,24	3,49	5,7	16,32	2,41	3,79	13,12
Endotoxin 2	1,07	0,94	0,99	2,88	6,57	3,4	2,69	6,99	3,43
Endotoxin 3	0,2	0,36	0,6	2,85	5,15	11,78	14,27	14,3	19,63
Endotoxin 4	1,08	0,77	2,25	2,11	8,36	16,11	1,96	10,9	7,16
Endotoxin 5	1,14	1,25	1,35	1,66	2,56	4,95	1,45	2,05	3,68
Endotoxin 6	0,88	1,42	1,79	3,73	9,7	15,73	4,22	6,83	8,8
Endotoxin 7	0,55	1,31	1,79	2,51	7,31	7,39	4,53	5,57	4,14
Endotoxin 8	1,29	1,46	1,94	3,29	4,56	6,56	2,56	3,12	3,38
Endotoxin 9	2,06	2,09	2,6	4,02	7,12	10,36	1,95	3,41	3,99
MEDIAN	*1,08*	*1,31*	*1,79*	*2,88*	*6,57*	*10,36*	*2,56*	*5,57*	*4,14*
RIQ1	*0,88*	*0,94*	*1,24*	*2,51*	*5,15*	*6,56*	*1,96*	*3,41*	*3,68*
RIQ3	*1,29*	*1,46*	*1,94*	*3,49*	*7,31*	*15,73*	*4,22*	*6,99*	*8,80*
Control 1	0,68	0,44	0,68	3,01	2,13	1,17	4,43	4,88	1,72
Control 2	1,21	1,6	1,25	2,36	1,2	2,42	1,95	0,75	1,93
Control 3	0,55	0,54	0,49	5,49	8,53	3,52	9,93	15,71	7,18
Control 4	1,43	1,39	1,39	1,36	1,83	1,38	0,95	1,32	0,99
MEDIAN	*0,94*	*0,97*	*0,97*	*2,68*	*1,98*	*1,9*	*3,19*	*3,1*	*1,83*
RIQ1	0,65	0,52	0,63	2,11	1,67	1,33	1,72	1,17	1,54
RIQ3	1,26	1,44	1,29	3,63	3,73	2,7	5,8	7,58	3,24

Table S6. Individual data of tricarboxylic acid cycle intermediates adjusted by hematocrit to derive blood concentrations.

	CITRATE µM/L			KETOGLUTARATE µM/L			SUCCINATE µM/L			FUMARATE µM/L			MALATE µM/L		
Animal Nº	**T0**	**T3**	**T6**	**T0**	**T3**	**T6**	**T0**	**T3**	**T6**	**T0**	**T3**	**T6**	**T0**	**T3**	**T6**
Endotoxin 1	193,17	258,13	300,00	50,83	66,13	42,00	46,77	503,47	778,00	1,28	3,18	2,53	0,83	0,89	3,32
Endotoxin 2	119,70	208,80	209,30	18,90	36,00	36,80	191,10	914,40	62,10	3,23	3,10	1,17	0,17	0,21	0,28
Endotoxin 3	156,40	73,60	602,80	27,20	29,90	72,60	272,00	278,30	701,80	2,07	1,59	43,49	0,17	0,31	0,34
Endotoxin 4	6,90	74,80	10,67	27,60	20,40	21,33	255,30	328,10	372,80	3,63	7,12	6,05	0,30	0,02	0,47
Endotoxin 5	112,80	365,00	394,20	41,40	45,63	51,10	369,60	428,27	615,03	2,68	4,50	2,99	0,63	0,40	0,49
Endotoxin 6	225,60	130,67	376,97	28,80	56,00	75,90	5,21	452,67	434,70	2,64	36,75	8,74	0,29	0,94	2,65
Endotoxin 7	33,13	2543,80	305,30	156,20	32,20	44,97	508,83	181,70	497,00	1,99	3,04	5,28	0,58	0,66	0,58
Endotoxin 8	718,67	227,20	287,04	48,77	61,53	82,80	269,50	492,27	540,50	33,08	4,89	4,85	0,88	1,15	0,89
Endotoxin 9	122,40	158,67	226,67	60,00	54,40	52,13	292,80	471,47	439,73	3,55	2,86	3,01	0,60	1,03	0,73
MEDIAN	122,40	208,80	300,0*†	41,40	45,63	51,10	269,50	452,67	497,0*†	2,68	3,18	4,85	0,58	0,66	0,58
RIQ1	72,97	102,73	217,98	27,40	31,05	39,40	118,93	303,20	403,75	2,03	2,95	2,76	0,23	0,26	0,41
RIQ3	209,38	311,57	385,58	55,42	58,77	74,25	331,20	497,87	658,41	3,59	6,00	7,39	0,73	0,98	1,77
Control 1	5,90	27,20	53,25	31,47	28,90	49,70	358,13	212,50	229,54	1,68	0,54	2,25	0,92	0,79	0,85
Control 2	154,80	299,27	126,00	33,60	40,20	58,33	871,20	591,83	112,00	4,37	5,09	3,45	0,40	0,48	0,39
Control 3	222,50	23,00	180,60	310,0	131,10	109,20	130,00	108,05	98,70	2,75	2,92	5,25	1,38	1,16	1,13
Control 4	234,37	149,33	142,00	168,5	165,67	189,33	347,60	361,67	321,87	3,31	44,47	47,29	0,48	0,44	0,46
MEDIAN	188,65	88,27	134,00	101,0	85,65	83,77	352,87	287,08	170,77	3,03	4,01	4,35	0,70	0,63	0,66
RIQ1	43,13	24,05	71,44	32,00	31,73	51,86	184,40	134,17	102,03	1,95	1,13	2,55	0,42	0,45	0,41
RIQ3	231,40	261,78	170,95	274,6	157,03	169,30	742,93	534,29	298,79	4,10	34,63	36,78	1,26	1,07	1,06

Differences between groups at each time point were obtained by the Mann–Whitney U test, and differences in the same group at different times were obtained by repeated-measures analysis of variance (ANOVA) with Bonferroni correction: * $p<0.05$ at T6 control vs endotoxin, † $p<0.05$ T0 vs T6 control vs endotoxin.