Supplementary Material

Methods

Immunoblotting for anti-cystathionine-γ-lyase (CSE; St John's Laboratory, London, UK) was performed as described previously (Hartmann et al. 2018). Primary antibodies were detected by using horseradish peroxidase-conjugated secondary antibodies (Cell Signaling, Danvers, MA, USA or Santa Cruz, Dallas, TX, USA). Anti-β-actin (Santa Cruz, Dallas, TX, USA) served as a loading control. Densitometry measurements were performed using NIH Image J software (http://rsb.info.nih.gov/nih-image), results are presented as densitometric sum.

Supplemental Tables

Table S1: Systemic physiologic parameters, as previously published in [20].

			baseline	24 h	Ref. Value
NoA ($\mu g \cdot kg^{-1} \cdot min^{-1}$)*	Sham	n=5	0.06 (0.02; 0.13)		n.a.
	sepsis	n=6	1.23 (0.66; 3.26)[b]		
Hemoglobin (g/dl)	sham	n=5	8.8 (8.6; 9.4)	9.2 (9.1; 9.8)	12.3-15.3
	sepsis	n=8	8.9 (8.5; 9.7)	11.7 (11.1; 12.3)[a,b]	
Heart rate (bpm)	sham	n=5	88 (73; 104)	102 (68; 115)	< 160
	sepsis	n=8	88 (74; 106)	156 (140; 166)[a,b]	
Mean arterial pressure (mmHg)	sham	n=5	100 (90; 106)	103 (94; 119)	max. +/- 10% of baseline
	sepsis	n=8	103 (91; 112)	65 (61; 81)[a,b]	
Central venous pressure (mmHg)	sham	n=5	8 (7; 13)	10 (9; 15)[a]	< 18
	sepsis	n=8	10 (6; 13)	17 (14; 18)[a]	
Cardiac output ($ml \cdot kg^{-1} \cdot min^{-1}$)	sham	n=5	61 (52; 79)	64 (42; 92)	n.a.
	sepsis	n=8	64 (52; 69)	87 (62; 130)[a]	
PaO_2 (mmHg)	sham	n=5	158 (142; 180)	159 (138;177)	n.a.[#]
	sepsis	n=8	170 (161; 183)	93 (62; 155)[a,b]	
$PaCO_2$ (mmHg)	sham	n=5	35 (35; 39)	35 (33; 36)	35-40
	sepsis	n=8	38 (34; 40)	35 (32; 44)	
arterial pH	sham	n=5	7.46 (7.44; 7.46)	7.44 (7.43; 7.46)	7.35-7.45
	sepsis	n=8	7.45 (7.43; 7.48)	7.37 (7.19; 7.43)[a,b]	
Base excess (mmol/l)	sham	n=5	1.1 (0.8; 1.8)	-0.1(-1.45; 0.65)	-2.0 to +2.0
	sepsis	n=8	1.5 (0.4; 2.3)	-8.5 (-14.6; -3.7) [a,b]	
Lactate (mmol/l)	sham	n=5	1.4 (1.0; 1.6)	0.6 (0.6; 1.2)	< 2.0
	sepsis	n=8	0.8 (0.6; 1.5)	6.1 (2.0; 10.7) [a,b]	

Data given as median (interquartile range). * NoA is administered based on mean arterial pressure (see Methods section) during the septic shock, # mechanical ventilation adjusted according to our previous work (if PaO_2/FiO_2 < 300mmHg = inspiratory/expiratory ratio 1:1, PEEP 12cm H_2O; if PaO_2/FiO_2 < 200mmHg = PEEP 15cm H_2O [10,19,26]), a $p<0.05$ in comparison to baseline, b $p<0.05$ in comparison to sham in two-way ANOVA

Table S2: Renal vein blood analysis, as previously published in [19,26].

		baseline	24h peritonitis
O_2 saturation (%)	sham	83 (81; 83)	83 (78; 84)
	sepsis	84 (78; 87)	66 (45; 83)
pH	sham	7.45 (7.44; 7.45)	7.42 (7.42; 7.44)
	sepsis	7.42 (7.42; 7.44)	7.28 (7.12; 7.36)[a,b]
Base excess (mmol/l)	sham	1.8 (1.8; 2.4)	1.1 (0.7; 1.2)

	sepsis	1.8 (1.0; 3.1)	-4.9 (-12.0; -2.2)[a,b]
Lactate (mmol/l)	sham	1.1 (1.0; 1.2)	1.0 (0.7; 1.2)
	sepsis	1.0 (0.7; 1.4)	4.7 (2.5; 8.9)[a,b]
IL6 (ng/$g_{protein}$)	sham	1.7 (1.3; 1.7)	6.9 (1.7; 7.9)
	sepsis	2.0 (1.8; 2.1)	1153.4 (236.4; 2002.5)[a,b]
TNFα (ng/$g_{protein}$)	sham	0.8 (0.6; 1.2)	1.6 (1.3; 2.0)
	sepsis	0.8 (0.7; 1.2)	15.3 (5.9; 21.7)[a,b]

Data given as median (interquartile range). a $p<0.05$ in comparison to baseline, b $p<0.05$ in comparison to sham in two-way ANOVA

Table S3: R^2 values for correlations with (unpooled) separate groups, respectively.

	CrCl (ml/min)		OxPhos jO_2 (pmol·s^{-1}·mg^{-1})		PGC1α expression		albumin extravasation		nitrotyrosine formation	
	sham	sepsis	sham	sepsis	sham	sepsis	sham	sepsis	sham	sepsis
NoA infusion (µg·kg^{-1}·min^{-1})	0.36	0.49	n.a.	1						
OxPhos jO_2 (pmol·s^{-1}·mg^{-1})	n.a.	0.89								
CSE expression	0.86	0.20	0.24	0.62	0.57	0.09	0.73	0.02	0.02	0.47
nitrotyrosine formation			0.85	0.84						

Supplemental Figure S1

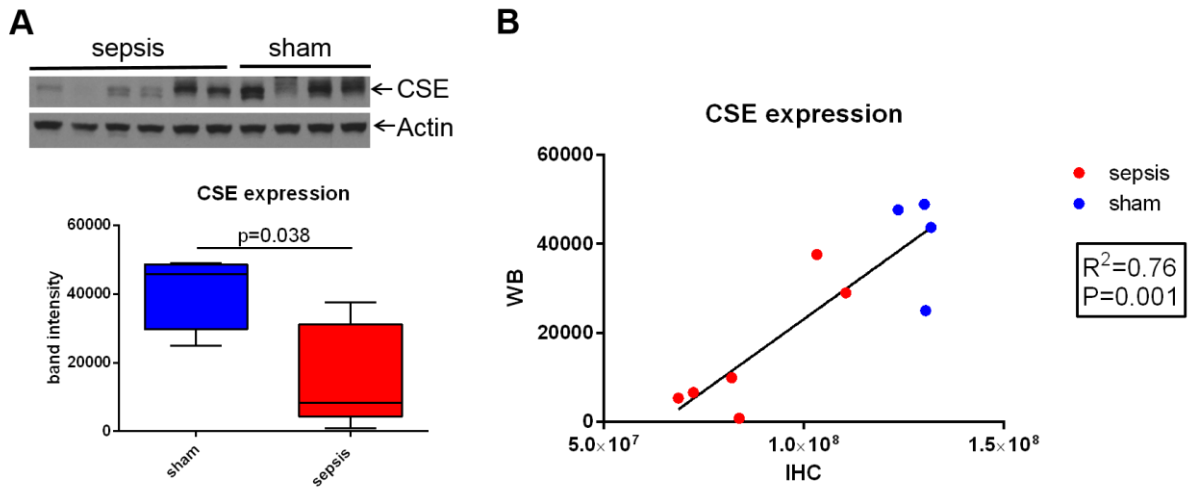

Figure S1: Kidney CSE protein expression levels for sham vs. sepsis, detected by western blot (WB, **A**) correlate with kidney CSE expression levels detected by immunohistochemistry (IHC, **B**).

References

Hartmann C, Gröger M, Noirhomme JP, Scheuerle A, Möller P, Wachter U, Huber-Lang M Nussbaum B, Jung B, Merz T, McCook O, Kress S, Stahl B, Calzia E, Georgieff M, Radermacher P, Wepler M. In-Depth Characterization of the Effects of Cigarette Smoke Exposure on the Acute Trauma Response and Hemorrhage in Mice. Shock. 2018. Volume Publish Ahead of Print.