





Figure S1. Analysis of variance for two groups of repeated data*.

* Plus minus values are means \pm SD. WBC denotes white blood cell, RBC red blood cell, Hb hemoglobin, PLT blood platelet, PT prothrombin time, APTT activated partial thromboplastin time, FIB fibrinogen, BUN blood urea, Cre serum creatinine, GRF glomerular filtration rate, ALT alanine aminotransferase, AST aspartate aminotransferase, TP total protein, ALB albumin, TBIL total bilirubin, DBIL direct bilirubin, IDBIL indirect bilirubin, Lac lactate, CRP C-reactive protein, PCT procalcitonin, SG specific gravity of urine, and SOFA sequential organ failure assessment.

Table S1. Analysis of variance for two groups of repeated data*

	Aminophylline group (n=50)						Usual-care group (n=46)						<i>P</i> value		
	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	time	Interaction effect	group
WBC - 10 ⁹ /L	13.16 ± 7.40	12.69 ± 6.21	12.29 ± 6.17	10.94 ± 4.89	10.93 ± 5.06	12.16 ± 6.77	14.87 ± 10.01	13.88 ± 9.40	13.40 ± 8.21	12.66 ± 6.27	12.01 ± 5.68	11.43 ± 6.17	0.079	0.180	0.377
RBC - 10 ¹² /L	3.50 ± 0.87	3.39 ± 0.69	3.34 ± 0.65	3.28 ± 0.63	3.28 ± 0.57	3.30 ± 0.61	3.43 ± 0.89	3.31 ± 0.81	3.27 ± 0.75	3.26 ± 0.63	3.29 ± 0.66	3.31 ± 0.72	0.084	0.957	0.767
Hb - g/L	103.08 ± 32.16	101.08 ± 22.52	99.63 ± 19.64	97.49 ± 18.24	97.99 ± 17.38	98.28 ± 16.95	103.31 ± 26.02	99.84 ± 22.91	98.19 ± 21.43	98.10 ± 18.33	98.91 ± 19.08	99.05 ± 20.61	0.251	0.954	0.995
PLT - 10 ⁹ /L	181.52 ± 130.08	180.54 ± 128.99	183.86 ± 143.66	196.68 ± 148.79	211.24 ± 160.80	233.36 ± 161.95	138.70 ± 106.47	138.33 ± 108.48	143.46 ± 111.70	158.04 ± 120.09	163.98 ± 118.50	165.39 ± 118.80	0.000	0.243	0.070
PT - s	13.53 ± 2.12	13.35 ± 2.24	15.61 ± 19.25	12.93 ± 2.78	13.09 ± 3.02	14.54 ± 9.24	14.04 ± 2.94	13.69 ± 4.04	14.24 ± 4.08	13.90 ± 4.55	13.63 ± 2.78	13.17 ± 1.92	0.567	0.485	0.932
APTT - s	34.48 ± 8.52	35.78 ± 12.63	34.31 ± 13.37	34.94 ± 14.18	35.82 ± 16.64	33.67 ± 9.98	35.99 ± 9.53	34.70 ± 8.39	40.75 ± 40.26	35.33 ± 12.06	34.64 ± 8.01	35.17 ± 7.75	0.312	0.552	0.559

FIB – g/L	5.35 ±4.17	4.86 ±1.79	4.77 ±1.71	4.44 ±1.56	4.28 ±1.60	4.08 ±1.55	4.07 ±1.92	4.08 ±1.69	4.41 ±2.71	3.91 ±1.88	3.80 ±1.88	3.80 ±1.83	0.004	0.474	0.062
D-dimer - mg/L	2.85 ±3.11	3.26 ±4.10	3.51 ±3.64	3.13 ±3.93	3.39 ±4.44	2.92 ±2.55	4.06 ±5.84	3.38 ±3.84	3.32 ±6.06	3.22 ±3.86	2.74 ±3.11	3.46 ±7.41	0.972	0.209	0.769
BUN – mmol/L	22.84 ±80.16	10.05 ±7.20	9.32 ±6.40	9.50 ±5.82	9.30 ±6.01	10.66 ±8.16	12.84 ±12.27	12.43 ±12.72	11.09 ±8.78	9.77 ±6.29	14.91 ±26.08	9.26 ±5.57	0.155	0.097	0.930
CREA – umol/L	139.92 ±140.95	138.73 ±171.78	107.41 ±91.32	99.72 ±70.40	96.25 ±73.68	97.64 ±75.70	135.96 ±143.88	118.27 ±135.48	104.32 ±110.87	97.54 ±101.27	97.59 ±103.01	96.06 ±103.95	0.015	0.863	0.804
GRE – ml/min	78.80 ±55.47	80.95 ±39.61	83.57 ±37.33	83.84 ±36.48	86.90 ±34.62	87.57 ±35.16	75.69 ±39.06	86.77 ±40.92	87.16 ±39.22	92.11 ±39.35	90.78 ±37.46	89.76 ±35.73	0.113	0.258	0.632
ALT – U/L	47.12 ±47.63	51.12 ±55.54	50.03 ±52.55	55.78 ±65.96	53.52 ±75.02	98.69 ±320.98	136.23 ±460.48	86.39 ±256.22	79.19 ±173.89	72.62 ±137.93	70.62 ±115.56	65.64 ±104.64	0.614	0.160	0.392
AST – U/L	61.27 ±76.74	78.61 ±133.00	68.43 ±115.81	81.44 ±166.19	64.45 ±121.08	161.37 ±686.85	225.46 ±900.85	98.73 ±264.84	74.53 ±120.87	61.60 ±80.07	55.30 ±61.91	53.02 ±54.89	0.307	0.181	0.820
TP – g/L	57.74 ±13.60	55.02 ±9.90	57.44 ±9.33	59.02 ±8.33	60.57 ±8.96	61.02 ±8.20	55.60 ±14.29	57.23 ±9.45	58.35 ±8.88	58.95 ±8.99	59.80 ±9.27	60.57 ±9.04	0.000	0.271	0.975
ALB - g/L	28.29 ±10.42	26.65 ±5.70	28.48 ±4.54	28.66 ±4.20	30.25 ±4.65	30.34 ±4.43	26.90 ±7.10	27.15 ±6.29	28.50 ±4.79	29.05 ±4.98	29.25 ±4.22	29.44 ±4.59	0.000	0.362	0.652
TBIL – umol/L	25.50 ±28.31	26.36 ±33.88	25.68 ±34.95	26.06 ±33.89	27.08 ±33.28	22.20 ±24.25	27.70 ±29.98	27.26 ±31.38	27.62 ±34.72	27.90 ±35.78	27.22 ±34.77	26.39 ±33.86	0.580	0.878	0.762
DBIL - umol/L	15.81 ±19.99	18.51 ±29.16	17.36 ±27.49	14.97 ±23.45	14.70 ±18.70	13.08 ±15.29	20.32 ±27.11	19.29 ±26.71	19.55 ±30.26	19.72 ±28.70	17.62 ±26.76	16.22 ±22.67	0.227	0.507	0.521

IDBIL - umol/L	6.95 ±5.80	6.63 ±7.41	6.79 ±6.00	7.31 ±6.82	6.78 ±6.09	7.08 ±5.70	7.17 ±5.57	7.10 ±7.42	6.88 ±7.55	6.90 ±7.77	7.62 ±8.48	7.87 ±8.83	0.904	0.831	0.792
PH	7.41 ±0.08	7.44 ±0.08	7.44 ±0.07	7.45 ±0.06	7.45 ±0.06	7.46 ±0.05	7.40 ±0.09	7.41 ±0.07	7.44 ±0.06	7.44 ±0.08	7.46 ±0.08	7.46 ±0.08	0.000	0.278	0.352
Lac – mmol/L	1.79 ±0.90	1.93 ±0.92	1.92 ±1.36	2.22 ±2.98	1.87 ±1.47	1.74 ±1.03	2.27 ±2.19	1.80 ±1.33	1.65 ±1.15	1.84 ±1.10	1.72 ±1.28	1.73 ±1.06	0.620	0.174	0.724
CRP - mg/L	160.42 ±82.47	156.56 ±88.89	115.16 ±74.11	93.89 ±76.37	91.67 ±79.01	72.11 ±67.05	157.84 ±128.32	146.37 ±101.34	120.40 ±93.71	111.70 ±98.07	93.77 ±89.89	85.44 ±79.01	0.000	0.121	0.753
PCT - g/ml	17.93 ±28.01	21.91 ±51.90	15.11 ±41.63	6.58 ±11.97	4.86 ±8.04	3.75 ±5.93	13.47 ±25.80	11.64 ±23.62	9.14 ±21.56	7.42 ±19.73	6.13 ±19.49	4.84 ±14.81	0.001	0.216	0.442
SG	1.02 ±0.01	1.02 ±0.01	1.02 ±0.01	1.02 ±0.01	1.02 ±0.01	1.02 ±0.01	1.02 ±0.01	1.02 ±0.01	1.02 ±0.01	1.02 ±0.01	1.02 ±0.01	1.02 ±0.01	0.987	0.713	0.864
SOFA	8.38 ±3.52	7.54 ±3.27	6.90 ±3.44	6.28 ±3.59	6.08 ±3.57	5.34 ±3.58	7.91 ±3.90	7.76 ±3.95	7.33 ±4.05	7.20 ±4.16	6.43 ±4.29	6.33 ±3.84	0.000	0.012	0.565
fluid intake – ml/24hr	4456.66 ±1765.03	4241.82 ±1458.58	3879.74 ±1203.44	3841.98 ±1313.84	3654.26 ±1248.04	3535.50 ±957.62	4186.04 ±1531.35	4030.17 ±1186.57	3883.70 ±1252.77	3811.57 ±1074.10	3690.50 ±1098.24	3399.28 ±1029.53	0.000	0.804	0.600
Urine-output - ml/24hr	2994.76 ±1547.70	2985.18 ±1192.31	3123.40 ±1413.69	3198.20 ±1341.14	2977.44 ±1319.09	2984.30 ±1189.44	2337.85 ±1416.22	2621.48 ±1305.57	2704.33 ±1501.82	2942.72 ±1479.85	3010.30 ±1609.07	2711.20 ±1330.67	0.377	0.608	0.081
Fluid output - ml/24h	3595.94 ±1783.27	3822.26 ±1519.88	3849.44 ±1697.40	3950.96 ±1525.19	3329.28 ±1448.86	3365.32 ±1220.17	2983.07 ±1584.93	3417.48 ±1214.66	3795.48 ±1661.52	3669.09 ±1383.66	3793.30 ±1513.68	3405.37 ±1438.95	0.060	0.122	0.441
Oxygenation index	223.36 ±86.45	219.47 ±77.07	227.70 ±77.53	250.46 ±76.38	266.72 ±85.71	272.48 ±90.13	257.36 ±88.18	245.09 ±87.59	253.65 ±84.72	231.01 ±81.83	262.56 ±90.26	260.00 ±90.92	0.004	0.027	0.539

Heart rate	100.66 ±25.41	96.44 ±22.93	96.04 ±23.96	94.28 ±19.98	89.68 ±22.48	88.26 ±21.29	96.41 ±24.18	91.70 ±19.33	89.33 ±19.93	86.07 ±19.93	87.80 ±18.59	96.41 ±19.08	0.013	0.615	0.176
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* Plus minus values are means ± SD. WBC denotes white blood cell, RBC red blood cell, Hb hemoglobin, PLT blood platelet, PT prothrombin time, APTT activated partial thromboplastin time, FIB fibrinogen, BUN blood urea, Cre serum creatinine, GRF glomerular filtration rate, ALT alanine aminotransferase, AST aspartate aminotransferase, TP total protein, ALB albumin, TBIL total bilirubin, DBIL direct bilirubin, IDBIL indirect bilirubin, Lac lactate, CRP C-reactive protein, PCT procalcitonin, SG specific gravity of urine, and SOFA sequential organ failure assessment.

Table S1. Results of repeated data analysis in the shock subgroup*.

	Aminophylline group (n=28)						Usual-care group (n=27)						P value		
	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	time	Interaction effect	group
Norepinephrine, ug/(kg*min)	0.54 ±0.73	0.43 ±0.58	0.22 ±0.37	0.19 ±0.33	0.12 ±0.24	0.07 ±0.17	0.45 ±0.51	0.39 ±0.60	0.28 ±0.46	0.15 ±0.19	0.13 ±0.28	0.18 ±0.52	0.000	0.051	0.983
WBC (10 ⁹ /L)	12.32 ±7.42	12.75 ±6.85	12.64 ±6.91	10.57 ±5.16	10.28 ±5.07	12.24 ±7.75	15.72 ±12.26	14.24 ±10.01	13.99 ±9.63	12.32 ±7.52	11.09 ±5.81	10.50 ±5.51	0.075	0.239	0.503
RBC (10 ¹² /L)	3.42 ±0.96	3.40 ±0.79	3.30 ±0.71	3.22 ±0.64	3.26 ±0.58	3.30 ±0.61	3.24 ±0.99	3.18 ±0.85	3.12 ±0.85	3.15 ±0.68	3.21 ±0.69	3.37 ±0.71	0.082	0.572	0.590
Hb (g/L)	101.75 ±30.35	100.97 ±24.63	98.44 ±21.82	96.40 ±19.46	97.34 ±18.81	97.92 ±17.87	96.59 ±28.62	94.64 ±23.19	92.85 ±23.40	93.90 ±19.59	95.49 ±19.74	99.82 ±20.30	0.214	0.680	0.568
PLT (10 ⁹ /L)	164.79 ±125.68	160.86 ±123.29	162.96 ±141.87	160.36 ±146.04	172.07 ±162.05	193.57 ±155.57	115.78 ±89.09	108.35 ±87.03	109.13 ±86.50	114.35 ±95.96	128.96 ±99.01	122.70 ±85.92	0.068	0.424	0.107
PT (s)	13.64 ±2.32	13.40 ±2.53	13.08 ±2.70	13.17 ±3.01	13.13 ±2.95	15.54 ±11.77	14.84 ±3.26	14.41 ±5.17	15.09 ±5.15	14.85 ±6.01	13.93 ±3.28	13.47 ±2.08	0.201	0.434	0.399
APTT (s)	34.88 ±7.83	34.92 ±7.68	33.11 ±5.97	32.99 ±3.77	32.87 ±5.59	33.31 ±5.45	37.01 ±9.17	36.47 ±7.36	46.80 ±55.63	37.24 ±14.43	34.30 ±5.70	35.67 ±6.30	0.056	0.676	0.093
FIB (g/L)	5.47 ±5.27	4.83 ±1.90	4.61 ±1.90	4.23 ±1.71	4.08 ±1.72	3.97 ±1.73	3.20 ±1.40	3.22 ±1.40	3.79 ±3.31	3.01 ±1.40	2.90 ±1.29	2.94 ±1.46	0.023	0.748	0.003
D-dimer (mg/L)	3.59 ±3.79	4.24 ±5.13	4.03 ±3.79	2.78 ±2.89	3.17 ±2.70	3.10 ±2.59	3.75 ±4.51	2.98 ±2.91	2.26 ±2.45	2.49 ±2.00	2.68 ±3.14	4.39 ±10.28	0.329	0.105	0.646
BUN (mmol/L)	32.07 ±106.71	10.26 ±6.77	9.55 ±5.93	10.06 ±5.97	10.13 ±6.33	10.64 ±7.16	13.63 ±10.96	12.04 ±10.20	10.64 ±7.65	9.19 ±5.51	16.39 ±34.21	8.79 ±5.33	0.422	0.290	0.652
GREA	148.71	121.89	106.48	104.38	103.38	105.56	130.93	102.86	95.88	76.88	72.94	69.21	0.041	0.377	0.290

(umol/L)	±121.75	±93.31	±71.30	±67.06	±81.89	±85.33	±136.35	±125.01	±97.19	±68.12	±56.28	±41.87			
GRE	75.15	75.24	79.61	78.30	83.20	83.90	76.25	93.39	96.39	103.62	103.49	103.43	0.058	0.297	0.091
(mL/min)	±67.46	±40.82	±37.99	±37.81	±36.00	±37.33	±40.42	±38.82	±38.57	±38.72	±34.24	±33.02			
ALT (U/L)	48.08	50.15	53.06	62.24	64.54	140.31	210.80	119.81	108.12	91.50	86.80	79.34	0.456	0.249	0.396
	±54.77	±52.52	±59.60	±75.24	±93.56	±424.38	±643.28	±356.06	±239.27	±184.74	±142.44	±121.49			
AST (U/L)	67.64	85.31	83.41	104.98	84.19	240.01	389.57	141.53	96.20	79.60	69.33	60.71	0.598	0.360	0.691
	±94.54	±145.85	±148.12	±216.98	±158.97	±910.18	±1263.98	±368.01	±156.21	±105.04	±77.05	±68.68			
TP (g/L)	56.49	53.76	56.50	57.53	58.48	60.11	54.26	53.95	54.74	56.29	57.80	57.68	0.004	0.773	0.508
	±9.05	±9.36	±8.39	±7.01	±7.00	±6.76	±12.42	±9.82	±8.85	±9.21	±8.82	±10.04			
ALB (g/L)	26.99	26.05	27.20	27.61	28.94	29.34	25.97	25.33	27.49	28.64	28.81	29.20	0.006	0.813	0.917
	±6.94	±5.80	±4.75	±4.02	±3.97	±4.44	±5.75	±5.26	±4.70	±5.75	±4.55	±5.25			
TBIL (umol/L)	25.84	30.51	28.64	26.49	27.02	24.95	30.21	33.85	35.67	34.54	34.45	33.28	0.399	0.952	0.530
	±28.57	±39.84	±40.03	±38.49	±33.65	±29.03	±27.60	±38.48	±44.63	±45.42	±45.48	±44.45			
DBIL (umol/L)	17.09	21.05	19.24	17.79	17.96	15.74	22.80	24.69	25.95	24.90	22.53	20.89	0.595	0.731	0.484
	±23.99	±33.30	±29.83	±29.69	±23.35	±18.16	±23.78	±32.02	±38.58	±35.25	±33.64	±27.05			
IDBIL (umol/L)	7.16	7.70	6.95	7.35	7.19	7.63	7.03	7.62	8.22	8.08	8.72	9.43	0.838	0.808	0.697
	±6.26	±9.28	±6.77	±7.39	±6.96	±6.69	±6.51	±9.48	±9.98	±10.45	±11.06	±11.82			
PH	7.41	7.44	7.44	7.45	7.46	7.46	7.38	7.41	7.43	7.47	7.49	7.49	0.000	0.142	0.741
	±0.09	±0.08	±0.07	±0.07	±0.07	±0.06	±0.10	±0.07	±0.08	±0.06	±0.07	±0.08			
Lac (mmol/L)	1.98	2.15	2.21	2.90	2.20	1.93	2.83	2.05	2.11	2.23	2.09	2.15	0.723	0.102	0.966
	±0.99	±1.05	±1.64	±3.83	±1.83	±1.17	±2.64	±1.64	±1.42	±1.38	±1.65	±1.25			
CRP (mg/L)	167.90	168.42	118.37	93.69	88.49	78.71	183.93	156.09	107.24	95.65	74.54	67.61	0.000	0.635	0.773
	±80.61	±99.28	±81.11	±79.86	±79.65	±74.99	±140.51	±119.76	±68.26	±59.02	±50.40	±55.14			
PCT (g/mL)	19.53	31.93	22.17	8.73	6.24	4.31	23.98	17.13	12.26	9.06	6.79	1.68	0.002	0.301	0.553
	±28.49	±67.46	±54.59	±15.11	±9.63	±6.13	±33.36	±26.93	±24.04	±20.90	±20.50	±1.62			
SG	1.02	1.02	1.02	1.02	1.02	1.02	1.02	1.02	1.02	1.02	1.02	1.02	0.654	0.322	0.353

	±0.02	±0.01	±0.01	±0.00	±0.01	±0.01	±0.01	±0.01	±0.00	±0.01	±0.00	±0.00			
SOFA	10.14	9.00	8.25	7.54	7.29	6.46	10.04	9.52	8.96	8.39	7.35	7.39	0.000	0.084	0.642
	±3.49	±3.38	±3.76	±3.97	±3.92	±4.06	±4.16	±4.48	±4.71	±4.62	±4.73	±3.94			
fluid intake	4965.43	4646.39	4220.64	4168.29	3923.04	3748.82	4498.48	4614.83	4308.83	4303.61	4088.52	3794.57	0.008	0.882	0.967
(mL/24h)	±1849.69	±1603.58	±1165.62	±1407.48	±1528.81	±1056.82	±1683.66	±1197.67	±1082.13	±800.37	±978.86	±852.93			
Urine-output	2934.86	2830.89	3072.64	3360.71	3029.54	3116.07	2351.70	2595.30	3030.78	3485.04	3234.35	2763.91	0.109	0.721	0.559
(mL/24h)	±1821.67	±1283.20	±1482.18	±1561.95	±1486.30	±1366.87	±1422.92	±1310.75	±1627.29	±1432.22	±1585.95	±1357.91			
Fluid output	3602.43	3813.00	3818.79	4230.21	3318.64	3471.21	2970.83	3406.61	4186.96	4258.22	3980.22	3439.48	0.020	0.335	0.993
(mL/24h)	±1925.92	±1714.78	±1954.12	±1638.28	±1583.54	±1368.94	±1569.48	±1159.06	±1462.57	±1230.52	±1445.12	±1629.45			
Oxygenation	246.46	238.59	235.60	265.10	262.31	269.16	256.37	245.97	261.38	260.33	292.40	279.95	0.290	0.356	0.466
index	±93.44	±71.12	±77.67	±76.60	±92.34	±96.25	±90.32	±74.05	±81.62	±75.36	±93.96	±103.38			

* Plus minus values are means ± SD. WBC: White blood cell; RBC: Red blood cell; Hb: Hemoglobin; PLTA: Blood platelet; PT: Prothrombin time; APTT: Activated partial thromboplastin time; FIB: Fibrinogen; BUN: Blood urea; Cre: Serum creatinine; GRF: Glomerular filtration rate; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; TP: Total protein; ALB: Albumin; TBIL: Total bilirubin; DBIL: Direct bilirubin; IDBIL: Indirect bilirubin; Lac: Lactate; CRP: C-reactive protein; PCT: Procalcitonin; SG: Specific gravity of urine; SOFA: Sequential organ failure assessment.

Table S2. Results of single-factor analysis.

Characteristics	Survival group (<i>n</i> = 74)	Death group (<i>n</i> = 26)	<i>P</i> Value
Group (aminophylline), <i>n</i>	41	9	0.043 ^a
Bloodstream infection, <i>n</i>	12	10	0.027 ^a
Ventilator application, <i>n</i>	27	17	0.020 ^a
Septic shock, <i>n</i>	32	23	<0.001 ^a
Hemoglobin-T0, mean (SD), g/L	105.24 (29.817)	95.12 (26.116)	0.080 ^b
Blood urea nitrogen-T0, median, (IQR),	8.27 (5.11–15.47)	13.75 (5.27–25.41)	0.195 ^c

	mmol/L		
Glomerular filtration rate-T0, median, (IQR), ml/min	72.48 (43.40–105.42)	96.00 (41.91–125.13)	0.183 ^c
Alanine aminotransferase-T0, median, (IQR), U/L	27.50 (18.00–74.50)	32.95 (15.50–57.50)	0.792 ^c
Total bilirubin, median-T0, (IQR), μmol/L	14.35 (10.20–29.28)	16.60 (7.90–40.55)	0.509 ^c
Blood lactate, median-T0, (IQR), mmol/L	1.50 (1.00–2.33)	1.70 (1.28–2.98)	0.103 ^c
APACHE II score-T0, median, (IQR)	15.00 (11.00–20.00)	16.50 (13.75–24.00)	0.108 ^c
SOFA score-T0, median, (IQR)	7.00 (5.00–10.00)	10.00 (6.75–15.00)	0.017 ^c
Fibrinogen-T0, median (IQR), g/L	4.26 (3.10–6.08)	4.15 (2.74–6.33)	0.622 ^c
D-Dimer-T0, median, (IQR), mg/L	1.94 (0.77–3.31)	2.44 (1.60–5.42)	0.096 ^c
Platelet count, median (IQR), ×10 ³ /μL	132.00 (64.5–212.75)	147.00 (74.25–251.75)	0.475 ^c

^a: chi-square. ^b: t-test. ^c: rank-sum test