

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

Characteristics	Aminophylline group (<i>n</i> =50)						Usual-care group (<i>n</i> =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	<0.001	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	<0.001	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	<0.001	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	<0.001	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	<0.001	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	<0.001	0.012	0.565
fluid intake (mL/24 h)	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	<0.001	0.804	0.600
Urine-output (mL/24 h)	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/24 h)	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

Date are presented as means ± standard deviation. WBC: 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; SOFA: Sequential organ failure assessment.

Table S2. Results of repeated data analysis in the shock subgroup.

Characteristics	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 ⁻¹ ·min ⁻¹)	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	<0.001	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	3.59	4.24	4.03	2.78	3.17	3.10	3.75	2.98	2.26	2.49	2.68	4.39	0.329	0.105	0.646

(mg/L)	±3.79	±5.13	±3.79	±2.89	±2.70	±2.59	±4.51	±2.91	±2.45	±2.00	±3.14	±10.28			
BUN (mmol/L)	32.07	10.26	9.55	10.06	10.13	10.64	13.63	12.04	10.64	9.19	16.39	8.79	0.422	0.290	0.652
	±106.71	±6.77	±5.93	±5.97	±6.33	±7.16	±10.96	±10.20	±7.65	±5.51	±34.21	±5.33			
GRE	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 (mL/min)	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
	±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	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
(umol/L)	±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	<0.001	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	<0.001	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	<0.001	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(mL/24h)	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
	±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 (mL/24h)	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
	±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 (mL/24h)	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
	±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 index	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
	±93.44	±71.12	±77.67	±76.60	±92.34	±96.25	±90.32	±74.05	±81.62	±75.36	±93.96	±103.38			

Date are presented as means ± standard deviation. WBC: 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; SOFA: Sequential organ failure assessment.