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

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

|                      | Aminophylline group (n=50) | Usual-care group (n=46) | 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 |
| WBC - 10^9/L         | 13.16  | 12.69  | 12.29  | 10.94  | 10.93  | 12.16  | 14.87  | 13.88  | 13.40  | 12.66  | 12.01  | 11.43  | 0.079 | 0.180 | 0.377 |
| RBC - 10^12/L        | ±7.40  | ±6.21  | ±6.17  | ±4.89  | ±5.06  | ±6.77  | ±10.01 | ±9.40  | ±8.21  | ±6.27  | ±5.68  | ±6.17  | 0.084 | 0.957 | 0.767 |
| Hb - g/L             | 3.50   | 3.39   | 3.34   | 3.28   | 3.28   | 3.30   | 3.43   | 3.31   | 3.27   | 3.26   | 3.29   | 3.31   | 0.251 | 0.954 | 0.995 |
| PT - s               | ±32.16 | ±22.52 | ±19.64 | ±18.24 | ±17.38 | ±16.95 | ±26.02 | ±22.91 | ±21.43 | ±18.33 | ±19.08 | ±20.61 | 0.000 | 0.243 | 0.070 |
| APTT - s             | 10.52  | ±13.08 | ±128.99| ±143.66| ±148.79| ±160.80| ±161.95| ±166.47| ±108.48| ±111.70| ±120.09| ±118.50| ±118.80| 0.567 | 0.485 | 0.932 |
|                      | ±34.48 | ±2.12  | ±9.24  | ±3.02  | ±2.94  | ±4.04  | ±4.55  | ±2.78  | ±1.92  | ±8.01  | ±7.75  | ±5.59  | 0.312 | 0.552 | 0.559 |

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.
| Parameter | Value | Standard Deviation | Minimum | Maximum |
|-----------|-------|--------------------|---------|---------|
| ALB (g/L) | ±19.99 | ±29.16 | ±27.49 | ±23.45 |
| TP (g/L)  | ±10.42 | ±5.70  | ±4.54  | ±4.20  |
| DBIL (umol/L) | ±15.81 | ±18.51 | ±17.36 | ±14.97 |
| TBIL (umol/L) | ±25.50 | ±26.36 | ±25.68 | ±26.06 |
| AST (U/L) | ±76.74 | ±133.00 | ±115.81 | ±166.19 |
| ALT (U/L) | ±47.12 | ±51.12 | ±50.03 | ±55.78 |
| CRE (umol/L) | ±140.95 | ±171.78 | ±91.32 | ±70.40 |
| GRE (ml/min) | ±55.47 | ±39.61 | ±37.33 | ±36.48 |
| FIB (g/L) | ±5.35  | ±4.86  | ±4.77  | ±4.44  |
| D-dimer (mg/L) | ±3.11  | ±4.10  | ±3.64  | ±3.93  |
| BUN (mmol/L) | ±22.84 | ±10.05 | ±9.32  | ±9.50  |
| FIB – g/L | 5.35  | ±4.17  | ±1.79  | ±1.71  |
| D-dimer - mg/L | ±3.11 | ±4.10  | ±3.64  | ±3.93  |
| BUN – mmol/L | ±22.84 | ±10.05 | ±9.32  | ±9.50  |
| CRE – umol/L | ±140.95 | ±171.78 | ±91.32 | ±70.40 |
| GRE – ml/min | ±55.47 | ±39.61 | ±37.33 | ±36.48 |
| ALT – U/L | ±47.12 | ±51.12 | ±50.03 | ±55.78 |
| AST – U/L | ±76.74 | ±133.00 | ±115.81 | ±166.19 |
| TP – g/L | ±57.74 | ±55.02 | ±57.44 | ±59.02 |
| ALB – g/L | ±28.29 | ±26.65 | ±28.48 | ±28.66 |
| TBIL – umol/L | ±25.50 | ±26.36 | ±25.68 | ±26.06 |
| DBIL – umol/L | ±15.81 | ±18.51 | ±17.36 | ±14.97 |
| IDBIL - umol/L | 6.95 | 6.63 | 6.79 | 7.31 | 6.78 | 7.08 | 7.17 | 7.10 | 6.88 | 6.90 | 7.62 | 7.87 | 0.904 | 0.831 | 0.792 |
|---------------|------|------|------|------|------|------|------|------|------|------|------|------|--------|--------|--------|
| ±               | ±5.80 | ±7.41 | ±6.00 | ±6.82 | ±6.09 | ±5.70 | ±5.57 | ±7.42 | ±7.55 | ±7.77 | ±8.48 | ±8.83 |        |        |        |
| PH            | 7.41 | 7.44 | 7.44 | 7.45 | 7.45 | 7.46 | 7.40 | 7.41 | 7.44 | 7.44 | 7.46 | 7.46 | 0.000 | 0.278 | 0.352 |
| ±               | ±0.08 | ±0.08 | ±0.07 | ±0.06 | ±0.06 | ±0.05 | ±0.09 | ±0.07 | ±0.06 | ±0.08 | ±0.08 | ±0.08 |        |        |        |
| Lac - mmol/L  | 1.79 | 1.93 | 1.92 | 2.22 | 1.87 | 1.74 | 2.27 | 1.80 | 1.65 | 1.84 | 1.72 | 1.73 | 0.620 | 0.174 | 0.724 |
| ±               | ±0.90 | ±0.92 | ±1.36 | ±2.98 | ±1.47 | ±1.03 | ±2.19 | ±1.33 | ±1.15 | ±1.10 | ±1.28 | ±1.06 |        |        |        |
| CRP - mg/L    | 160.42 | 156.56 | 115.16 | 93.89 | 91.67 | 72.11 | 157.84 | 146.37 | 120.40 | 111.70 | 93.77 | 85.44 | 0.000 | 0.121 | 0.753 |
| ±               | ±82.47 | ±88.89 | ±74.11 | ±76.37 | ±79.01 | ±67.05 | ±128.32 | ±101.34 | ±93.71 | ±98.07 | ±89.89 | ±79.01 |        |        |        |
| PCT - g/ml    | 17.93 | 21.91 | 15.11 | 6.58 | 4.86 | 3.75 | 13.47 | 11.64 | 9.14 | 7.42 | 6.13 | 4.84 | 0.001 | 0.216 | 0.442 |
| ±               | ±28.01 | ±51.90 | ±41.63 | ±11.97 | ±8.04 | ±5.93 | ±25.80 | ±23.62 | ±21.56 | ±19.73 | ±19.49 | ±14.81 |        |        |        |
| 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 | 0.987 | 0.713 | 0.864 |
| ±               | ±0.01 | ±0.01 | ±0.01 | ±0.01 | ±0.01 | ±0.01 | ±0.01 | ±0.01 | ±0.01 | ±0.01 | ±0.01 | ±0.01 |        |        |        |
| SOFA         | 8.38 | 7.54 | 6.90 | 6.28 | 6.08 | 5.34 | 7.91 | 7.76 | 7.33 | 7.20 | 6.43 | 6.33 | 0.000 | 0.012 | 0.565 |
| ±               | ±3.52 | ±3.27 | ±3.44 | ±3.59 | ±3.57 | ±3.58 | ±3.90 | ±3.95 | ±4.05 | ±4.16 | ±4.29 | ±3.84 |        |        |        |

| fluid intake | 4456.66 | 4241.82 | 3879.74 | 3841.98 | 3654.26 | 3535.50 | 4186.04 | 4030.17 | 3883.70 | 3811.57 | 3690.50 | 3399.28 | 0.000 | 0.804 | 0.600 |
| - ml/24hr     | ±1765.03 | ±1458.58 | ±1203.44 | ±1313.84 | ±1248.04 | ±957.62 | ±1531.35 | ±1186.57 | ±1252.77 | ±1074.10 | ±1098.24 | ±1029.53 |        |        |        |
| Urine-output  | 2994.76 | 2985.18 | 3123.40 | 3198.20 | 2977.44 | 2984.30 | 2337.85 | 2621.48 | 2704.33 | 2942.72 | 3010.30 | 2711.20 | 0.377 | 0.608 | 0.081 |
| - ml/24hr     | ±1547.70 | ±1192.31 | ±1413.69 | ±1341.14 | ±1319.09 | ±1189.44 | ±1416.22 | ±1305.57 | ±1501.82 | ±1479.85 | ±1609.07 | ±1330.67 |        |        |        |
| Fluid output  | 3595.94 | 3822.26 | 3849.44 | 3950.96 | 3329.28 | 3365.32 | 2983.07 | 3417.48 | 3795.48 | 3669.09 | 3793.30 | 3405.37 | 0.060 | 0.122 | 0.441 |
| - ml/24h      | ±1783.27 | ±1519.88 | ±1697.40 | ±1525.19 | ±1448.86 | ±1220.17 | ±1584.93 | ±1214.66 | ±1661.52 | ±1383.66 | ±1513.68 | ±1438.95 |        |        |        |
| Oxygenation index | 223.36 | 219.47 | 227.70 | 250.46 | 266.72 | 272.48 | 257.36 | 245.09 | 253.65 | 231.01 | 262.56 | 260.00 | 0.004 | 0.027 | 0.539 |
| Heart rate | 100.66 | 96.44 | 96.04 | 94.28 | 89.68 | 88.26 | 96.41 | 91.70 | 89.33 | 86.07 | 87.80 | 96.41 | 0.013 | 0.615 | 0.176 |
|------------|--------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| ±25.41     | ±22.93 | ±23.96| ±19.98| ±22.48| ±21.29| ±24.18| ±19.33| ±19.93| ±19.93| ±18.59| ±19.08|         |       |       |

* 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 | group |
| Norepinephrine, ug/(kg*min) | 0.54  | 0.43  | 0.22  | 0.19  | 0.12  | 0.07  | 0.45  | 0.39  | 0.28  | 0.15  | 0.13  | 0.18  | 0.000 | 0.051        | 0.983 |
| WBC (10^8/L)         | 12.32 | 12.75 | 12.64 | 10.57 | 10.28 | 12.24 | 15.72 | 14.24 | 13.99 | 12.32 | 11.09 | 10.50 | 0.075 | 0.239        | 0.503 |
| D-dimer (ug/L)       | 3.42  | 3.40  | 3.30  | 3.22  | 3.26  | 3.30  | 3.24  | 3.18  | 3.12  | 3.15  | 3.21  | 3.37  | 0.082 | 0.572        | 0.590 |
| Hb (g/L)             | 101.75| 100.97| 98.44 | 96.40 | 97.34 | 97.92 | 96.59 | 94.64 | 92.85 | 93.90 | 95.49 | 99.82 | 0.214 | 0.680        | 0.568 |
| PT (s)               | 13.64 | 13.40 | 13.08 | 13.17 | 13.13 | 15.54 | 14.84 | 14.41 | 15.09 | 14.85 | 13.93 | 13.47 | 0.201 | 0.434        | 0.399 |
| APTT (s)             | 34.88 | 34.92 | 33.11 | 32.99 | 32.87 | 33.31 | 37.01 | 36.47 | 46.80 | 37.24 | 34.30 | 35.67 | 0.056 | 0.676        | 0.093 |
| FIB (g/L)            | 5.47  | 4.83  | 4.61  | 4.23  | 4.08  | 3.97  | 3.20  | 3.22  | 3.79  | 3.01  | 2.90  | 2.94  | 0.023 | 0.748        | 0.003 |
| D-dimer (mg/L)       | 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 |
| BUN (mmol/L)         | 106.71| 67.77 | 5.93  | 5.97  | 6.33  | 7.16  | 10.96 | 10.20 | 7.65  | 5.51  | 34.21 | 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 (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 |
| ALT (U/L) | ±54.77 | ±52.52 | ±59.60 | ±75.24 | ±93.56 | ±424.38 | ±643.28 | ±356.06 | ±239.27 | ±184.74 | ±142.44 | ±121.49 |       |       |       |       |       |       | 0.456 | 0.249 | 0.396 |
| AST (U/L) | ±94.54 | ±145.85 | ±148.12 | ±216.98 | ±158.97 | ±910.18 | ±1263.98 | ±368.01 | ±156.21 | ±105.04 | ±77.05 | ±68.68 |       |       |       |       |       |       | 0.598 | 0.360 | 0.691 |
| TP (g/L) | ±9.05 | ±9.36 | ±8.39 | ±7.01 | ±7.00 | ±6.76 | ±12.42 | ±9.82 | ±8.85 | ±9.21 | ±8.82 | ±10.04 |       |       |       |       |       |       | 0.004 | 0.773 | 0.508 |
| ALB (g/L) | ±6.94 | ±5.80 | ±4.75 | ±4.02 | ±3.97 | ±4.44 | ±5.75 | ±5.26 | ±4.70 | ±5.75 | ±4.55 | ±5.25 |       |       |       |       |       |       | 0.006 | 0.813 | 0.917 |
| TBIL (umol/L) | ±28.57 | ±39.84 | ±40.03 | ±38.49 | ±33.65 | ±29.03 | ±27.60 | ±38.48 | ±44.63 | ±45.42 | ±45.48 | ±44.45 |       |       |       |       |       |       | 0.399 | 0.952 | 0.530 |
| DBIL (umol/L) | ±23.99 | ±33.30 | ±29.83 | ±29.69 | ±23.35 | ±18.16 | ±23.78 | ±32.02 | ±38.58 | ±35.25 | ±33.64 | ±27.05 |       |       |       |       |       |       | 0.595 | 0.731 | 0.484 |
| 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 |
| PH | ±0.09 | ±0.08 | ±0.07 | ±0.07 | ±0.07 | ±0.06 | ±0.10 | ±0.07 | ±0.08 | ±0.06 | ±0.07 | ±0.08 |       |       |       |       |       |       | 0.000 | 0.142 | 0.741 |
| 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 |
| CRP (mg/L) | ±80.61 | ±99.28 | ±81.11 | ±79.86 | ±79.65 | ±74.99 | ±140.51 | ±119.76 | ±68.26 | ±59.02 | ±50.40 | ±55.14 |       |       |       |       |       |       | 0.000 | 0.635 | 0.773 |
| PCT (g/mL) | ±28.49 | ±67.46 | ±54.59 | ±15.11 | ±9.63 | ±6.13 | ±33.36 | ±26.93 | ±24.04 | ±20.90 | ±20.50 | ±1.62 |       |       |       |       |       |       | 0.002 | 0.301 | 0.553 |
| 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 |
### Table S2. Results of single-factor analysis.

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

* 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.
| Test                              | T0 Median (IQR)     | T1 Median (IQR)     | P-value |
|-----------------------------------|---------------------|---------------------|---------|
| Glomerular filtration rate       | 72.48 (43.40–105.42)| 96.00 (41.91–125.13)| 0.183<sup>a</sup> |
| Alanine aminotransferase         | 27.50 (18.00–74.50  )| 32.95 (15.50–57.50  )| 0.792<sup>c</sup> |
| Total bilirubin                  | 14.35 (10.20–29.28)| 16.60 (7.90–40.55)  | 0.509<sup>c</sup> |
| Blood lactate                    | 1.50 (1.00–2.33)    | 1.70 (1.28–2.98)    | 0.103<sup>c</sup> |
| APACHE II score                  | 15.00 (11.00–20.00  )| 16.50 (13.75–24.00  )| 0.108<sup>c</sup> |
| SOFA score                       | 7.00 (5.00–10.00)   | 10.00 (6.75–15.00)  | 0.017<sup>c</sup> |
| Fibrinogen                       | 4.26 (3.10–6.08)    | 4.15 (2.74–6.33)    | 0.622<sup>c</sup> |
| D-Dimer                          | 1.94 (0.77–3.31)    | 2.44 (1.60–5.42)    | 0.096<sup>c</sup> |
| Platelet count                   | 132.00 (64.5–212.75)| 147.00 (74.25–251.75)| 0.475<sup>c</sup> |

<sup>a</sup>: chi-square.  <sup>b</sup>: t-test.  <sup>c</sup>: rank-sum test