Supplementary Table S1. Univariable regression analysis of the δ -platelet count

Variables	Regression coefficient	Standard error	p
Timing of antibiotic therapy (per hour delay) [†]	-1.860	0.771	0.016
Age (years) [†]	-0.212	0.101	0.035
Sex (male)	2.494	2.861	0.385
Comorbidities			
Hypertension	-1.975	2.952	0.504
Diabetes	4.095	3.253	0.209
Cardiac disease	-4.719	4.233	0.265
Chronic lung disease	-2.670	5.879	0.650
Chronic renal disease [†]	-16.900	6.364	0.008
Chronic liver disease [†]	14.784	5.131	0.004
Metastatic solid cancer	-1.237	3.371	0.714
Hematologic malignancy [†]	18.407	4.969	< 0.001
Suspected infectious focus			
Intra-abdominal	Reference		
Respiratory [†]	15.710	3.376	< 0.001
Urinary [†]	14.477	4.603	0.002
Other [†]	14.377	4.152	0.001
Positive blood cultures	0.253	2.885	0.930
Resistant bacterial infection	-5.121	5.142	0.319
APACHE II score [†]	-0.391	0.163	0.016
Laboratory results			
Initial lactate (mmol/L) [†]	-3.199	0.480	< 0.001
C-reactive protein (mg/dL) [†]	0.386	0.125	0.002
Interventions			
Fluid resuscitation within 3 hours (30 ml/kg)	-2.399	2.835	0.398
Fluid input within 24 hours (L) [†]	-4.166	0.671	< 0.001
Vasopressors [†]	-6.869	2.913	0.019

The total number of patients was 1525 for δ -platelet analysis after excluding if they had received platelet transfusions. Univariable linear regression analysis was used. †P-value <0.05 was considered statistically significant. APACHE, Acute Physiology and Chronic Health Evaluation.

Supplementary Table S2. Univariable regression analysis of the δ -serum bilirubin

Variables	Regression coefficient	Standard error	P
Timing of antibiotic therapy (per hour delay) [†]	0.044	0.021	0.031
Age (years)	-0.003	0.003	0.282
Sex (male)	0.088	0.077	0.249
Comorbidities			
Hypertension	0.025	0.079	0.755
Diabetes	-0.041	0.087	0.640
Cardiac disease	0.058	0.114	0.611
Chronic lung disease	-0.149	0.158	0.344
Chronic renal disease	0.196	0.171	0.251
Chronic liver disease	0.121	0.134	0.367
Metastatic solid cancer	0.157	0.090	0.082
Hematologic malignancy [†]	0.510	0.124	< 0.001
Suspected infectious focus			
Intra-abdominal [†]	Reference		
Respiratory	0.349	0.091	< 0.001
Urinary	0.237	0.123	0.055
Other [†]	0.370	0.110	0.001
Positive blood cultures	-0.105	0.077	0.173
Resistant bacterial infection [†]	-0.281	0.137	0.041
APACHE II score [†]	0.025	0.004	< 0.001
Laboratory results			
Initial lactate (mmol/L) [†]	0.084	0.013	< 0.001
C-reactive protein (mg/dL)	0.006	0.003	0.088
Interventions			
Fluid resuscitation within 3 hours (30 ml/kg)	0.099	0.076	0.192
Fluid input within 24 hours (L) [†]	0.068	0.018	< 0.001
Vasopressors [†]	0.261	0.078	0.001

The total number of patients was 1784. Univariable linear regression analysis was used. †P-value <0.05 was considered statistically significant. APACHE, Acute Physiology and Chronic Health Evaluation.

Supplementary Table S3. Univariable regression analysis of the δ -serum creatinine

Variables	Regression coefficient	Standard error	p
Timing of antibiotic therapy (per hour delay)	0.018	0.011	0.100
Age (years)	0.001	0.001	0.491
Sex (male)	0.030	0.040	0.453
Comorbidities			
Hypertension	-0.010	0.042	0.804
Diabetes	0.036	0.046	0.429
Cardiac disease	0.100	0.060	0.098
Chronic lung disease [†]	0.202	0.081	0.013
Chronic renal disease	0.090	0.121	0.460
Chronic liver disease	-0.013	0.071	0.856
Metastatic solid cancer	-0.014	0.046	0.762
Hematologic malignancy	0.112	0.065	0.085
Suspected infectious focus			
Intra-abdominal	Reference		
Respiratory [†]	0.185	0.047	< 0.001
Urinary	-0.074	0.063	0.244
Other	0.063	0.057	0.272
Positive blood cultures	-0.028	0.040	0.484
Resistant bacterial infection	-0.031	0.072	0.667
APACHE II score [†]	-0.005	0.002	0.029
Laboratory results			
Initial lactate (mmol/L)	-0.015	0.008	0.052
C-reactive protein (mg/dL) [†]	-0.015	0.002	< 0.001
Interventions			
Fluid resuscitation within 3 hours (30 ml/kg $^{\scriptsize \dagger}$	-0.230	0.039	<0.001
Fluid input within 24 hours (L) ⁺	-0.051	0.009	< 0.001
Vasopressors [†]	-0.185	0.040	< 0.001

The total number of patients was 1604 after excluding if they received renal replacement therapy. Univariable linear regression analysis was used. †P-value <0.05 was considered statistically significant. APACHE, Acute Physiology and Chronic Health Evaluation.

Supplementary Table S4. Univariable regression analysis of the δ - PaO₂/FiO₂ ratio

Variables	Regression coef	Regression coefficient Standard error	
Timing of antibiotic therapy (per hour delay	y)		
Age (years)	0.217	0.244	0.374
Sex (male)	-7.811	6.963	0.262
Comorbidities			
Hypertension	12.497	7.181	0.082
Diabetes [†]	19.039	7.917	0.016
Cardiac disease ⁺	22.246	10.321	0.031
Chronic lung disease	15.581	14.412	0.280
Chronic renal disease	8.324	15.487	0.591
Chronic liver disease	-3.122	12.211	0.798
Metastatic solid cancer [†]	-19.151	8.231	0.020
Hematologic malignancy	-0.242	11.267	0.983
Suspected infectious focus			
Intra-abdominal	Reference		
Respiratory [†]	19.156	8.288	0.021
Urinary	29.727	11.161	0.008^{+}
Other	13.946	10.060	0.166
Positive blood cultures [†]	-27.617	6.979	< 0.001
Resistant bacterial infection	15.794	12.589	0.210
APACHE II score [†]	1.884	.387	< 0.001
Laboratory results			
Initial lactate (mmol/L) [†]	-6.100	1.186	< 0.001
C-reactive protein (mg/dL)	-1.301	0.304	< 0.001
Interventions			
Fluid resuscitation within 3 hours (30 ml/kg) [†]	16.396	6.884	0.017
Fluid input within 24 hours (L) [†]	-9.503	1.636	< 0.001
Vasopressors [†]	-24.218	7.079	0.001

The total number of patients was 1780 after excluding patients with missing values. Univariable linear regression analysis was used. †P-value <0.05 was considered statistically significant. APACHE, Acute Physiology and Chronic Health Evaluation.