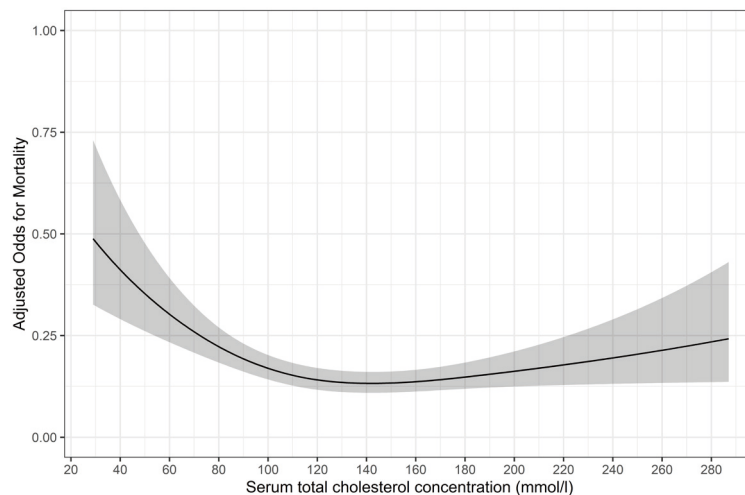


**Figure S1** The restricted cubic spline curve of mortality at 28 days according to the serum total cholesterol concentrations in patients enrolled from May 2014 to February 2016. Patients with severe sepsis and septic shock according to The Second International Sepsis Definition Consensus were enrolled during this period. The black line indicates the adjusted odds ratios for mortality at 28 days, and the gray shaded area represents the 95% confidence interval.



**Figure S2** The restricted cubic spline curve of mortality at 28 days according to the serum total cholesterol concentrations in patients enrolled from March 2016 to April 2018. Patients with sepsis and septic shock according to the Sepsis-3 definition were enrolled during this period. The black line indicates the adjusted odds ratios for mortality at 28 days, and the gray shaded area represents the 95% confidence interval.

**Table S1** Baseline characteristics of patients according to the study period

Variables	From May 2014 to February 2016	From March 2016 to April 2018	p
	(N=1,616)	(N=2,896)	
Age	73.0 (62.0–79.0)	73.0 (63.0–80.0)	0.037
Male	985 (61.0)	1724 (59.5)	0.366
Body mass index	21.3 (18.5–24.0)	21.3 (18.5–24.0)	0.813
Comorbidity			
Hypertension	678 (42.0)	1294 (44.7)	0.077
Diabetes	519 (32.1)	965 (33.4)	0.414
Chronic liver disease	165 (10.2)	230 (7.9)	0.011
Congestive heart failure	31 (1.9)	55 (1.9)	1.000
Chronic lung disease	194 (12.0)	316 (10.9)	0.290
Chronic kidney disease	142 (8.8)	288 (9.9)	0.224
Malignant disease	597 (36.9)	1138 (39.3)	0.127
Initial hemodynamic variables			
Mean arterial pressure (mmHg)	66.0 (58.0–80.0)	72.0 (60.0–90.0)	<0.001
Heart rate (beat/min)	107.0 (89.0–124.0)	102.0 (87.0–119.0)	<0.001
Respiratory rate (breath/min)	22.0 (18.0–26.0)	20.0 (18.0–24.0)	<0.001
Body temperature (°C)	37.2 (36.5–38.1)	37.3 (36.7–38.2)	<0.001
Laboratory results			
Total cholesterol (mg/dL)	116.0 (88.5–145.0)	120.0 (92.0–152.0)	0.002
White blood cell ( $10^3/\mu\text{L}$ )	11.3 (6.6–17.3)	11.1 (6.2–16.5)	0.186
Hemoglobin (g/dL)	10.9 (9.2–12.5)	11.1 (9.4–12.7)	0.031
Platelet ( $10^3/\mu\text{L}$ )	168.0 (99.5–246.0)	176.0 (102.0–259.0)	0.038
Creatinine (mg/dL)	1.3 (0.9–2.1)	1.2 (0.8–2.0)	0.081
Albumin (g/dL)	3.0 (2.6–3.4)	3.1 (2.6–3.5)	<0.001
Total bilirubin (mg/dL)	0.9 (0.6–1.5)	0.9 (0.6–1.7)	0.004
CRP (mg/dL)	13.1 (6.7–21.8)	12.4 (5.2–20.7)	0.004
Lactate (mmol/L)	2.5 (1.5–4.7)	2.4 (1.4–4.2)	0.012
Infection site			
Lung	746 (46.2)	1295 (44.7)	0.366
Urogenital	288 (17.8)	550 (19.0)	0.353
Intra-abdomen	440 (27.2)	768 (26.5)	0.631
Others	142 (8.8)	327 (11.3)	0.010
APACHE II score	23.0 (17.0–31.0)	19.0 (14.0–26.0)	<0.001
SOFA score	7.0 (5.0–10.0)	6.0 (4.0–9.0)	<0.001
28-day mortality	333 (20.6)	559 (19.3)	0.310

Data are expressed as median (interquartile range) or n (%) as appropriate. CRP, C-reactive protein; SOFA, Sequential Organ Failure Assessment; APACHE, Acute Physiology and Chronic Health Evaluation.