

**Table S1** The percentage of missing value of all the participants

Characteristics	Non-ondansetron (n=12,831)	Ondansetron (n=5,735)
<b>Demographic data</b>		
Age (years), mean (SD)	0 (0.00)	0 (0.00)
Gender (male), n (%)	0 (0.00)	0 (0.00)
Ethnicity (non-white), n (%)	0 (0.00)	0 (0.00)
Married, n (%)	0 (0.00)	0 (0.00)
Insurance (Medicare), n (%)	0 (0.00)	0 (0.00)
Admission type (emergency), n (%)	0 (0.00)	0 (0.00)
Weight (kg), median (IQR)	61 (0.48)	43 (0.75)
<b>Clinical data</b>		
White blood cell ( $\times 10^9$ ), median (IQR)	59 (0.46)	16 (0.28)
Platelet ( $\times 10^{12}$ ), median (IQR)	65 (0.51)	16 (0.28)
Creatinine (mg/dL), median (IQR)	58 (0.45)	13 (0.23)
Lactate (mmol/L), median (IQR)	2,295 (17.89)	861 (15.01)
SAPS II score, median (IQR)	0 (0.00)	0 (0.00)
SOFA score, median (IQR)	0 (0.00)	0 (0.00)
GCS score, median (IQR)	23 (0.18)	2 (0.03)
AKI, n (%)	0 (0.00)	0 (0.00)
<b>Medical history, n (%)</b>		
Hypertension	0 (0.00)	0 (0.00)
Diabetes	0 (0.00)	0 (0.00)
Chronic heart disease	0 (0.00)	0 (0.00)
CKD	0 (0.00)	0 (0.00)
Chronic liver disease	0 (0.00)	0 (0.00)
COPD	0 (0.00)	0 (0.00)
Malignancy	0 (0.00)	0 (0.00)
<b>Diagnosis, n (%)</b>		
Surgery	53 (0.41)	32 (0.56)
Sepsis	0 (0.00)	0 (0.00)
ACS/AMI	0 (0.00)	0 (0.00)
Pneumonia	0 (0.00)	0 (0.00)
<b>Treatments</b>		
Fluid input on day 2 (L), median (IQR)	37 (0.29)	10 (0.17)
CRRT, n (%)	0 (0.00)	0 (0.00)
Glucocorticoids, n (%)	0 (0.00)	0 (0.00)
Vasopressor use, n (%)	0 (0.00)	0 (0.00)
Metoclopramide, n (%)	0 (0.00)	0 (0.00)
<b>Antibiotics, n (%)</b>		
Carbapenems	0 (0.00)	0 (0.00)
Glycopeptide	0 (0.00)	0 (0.00)
$\beta$ -lactams	0 (0.00)	0 (0.00)
Aminoglycosides	0 (0.00)	0 (0.00)

SD, standard deviation; IQR, interquartile range; SAPS II, simplified acute physiology score II; SOFA, sequential organ failure assessment; GCS, Glasgow coma scale; AKI, acute kidney disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; ACS/AMI, acute coronary syndrome/acute myocardial infarction; CRRT, continuous renal replacement therapy.

**Table S2** Sensitivity analysis of association between ondansetron use within 48 h after ICU admission and outcomes.

Model	HR	95% CI	P
In-hospital mortality			
Unadjusted	0.38	0.38-0.42	<0.001
Multivariable	0.50	0.44-0.57	<0.001
IPTW	0.67	0.53-0.83	<0.001
PSM	0.53	0.46-0.60	<0.001
60-day mortality			
Unadjusted	0.36	0.32-0.41	<0.001
Multivariable	0.51	0.44-0.58	<0.001
IPTW	0.81	0.65-1.00	0.057
PSM	0.55	0.48-0.63	<0.001

Unadjusted: without adjustment; multivariable adjusted: adjusted for the baseline variables shown in *Table 1*. HR, hazard ratio; CI, confidence interval; IPTW, inverse probability treatment weighting; PSM, propensity score matching.